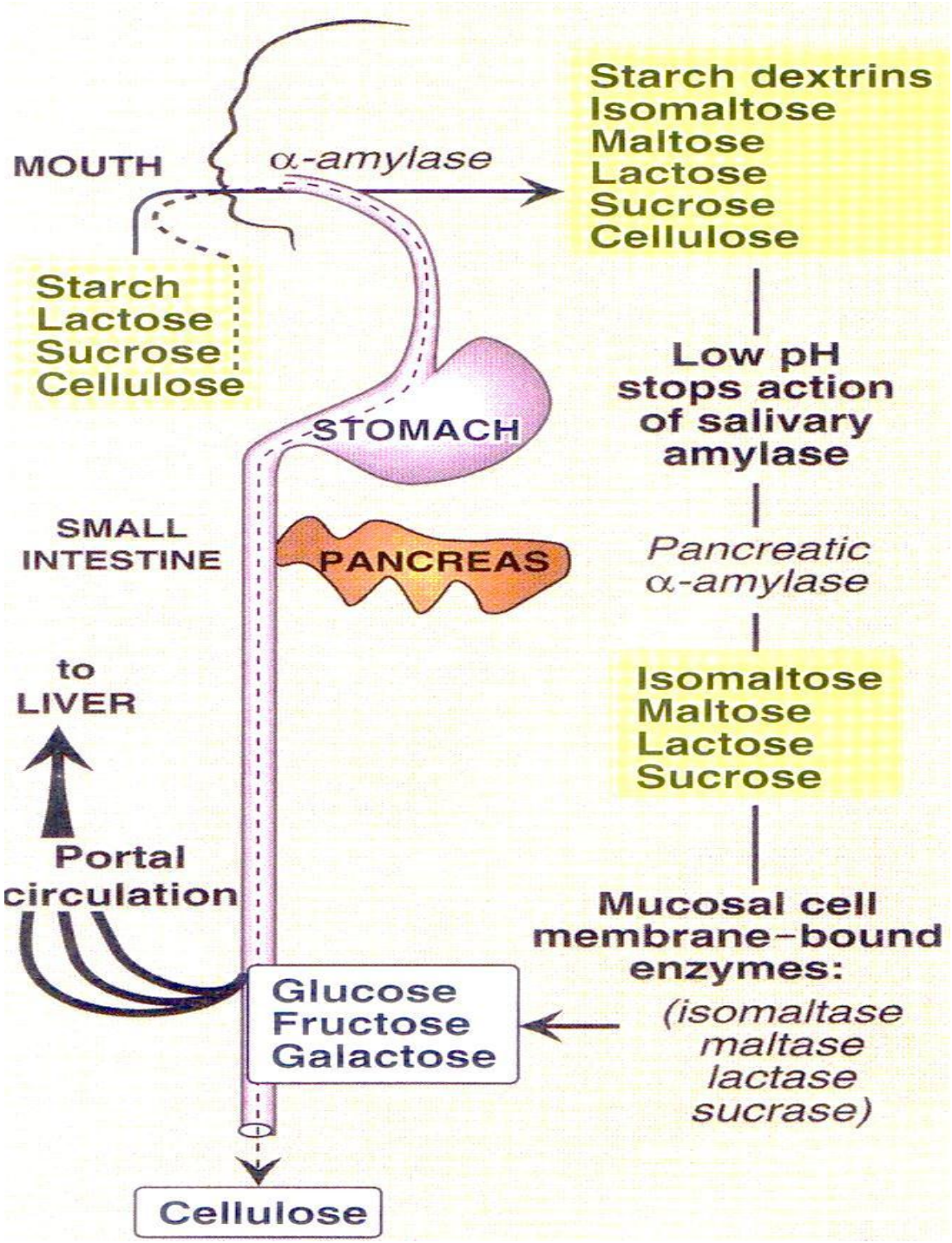
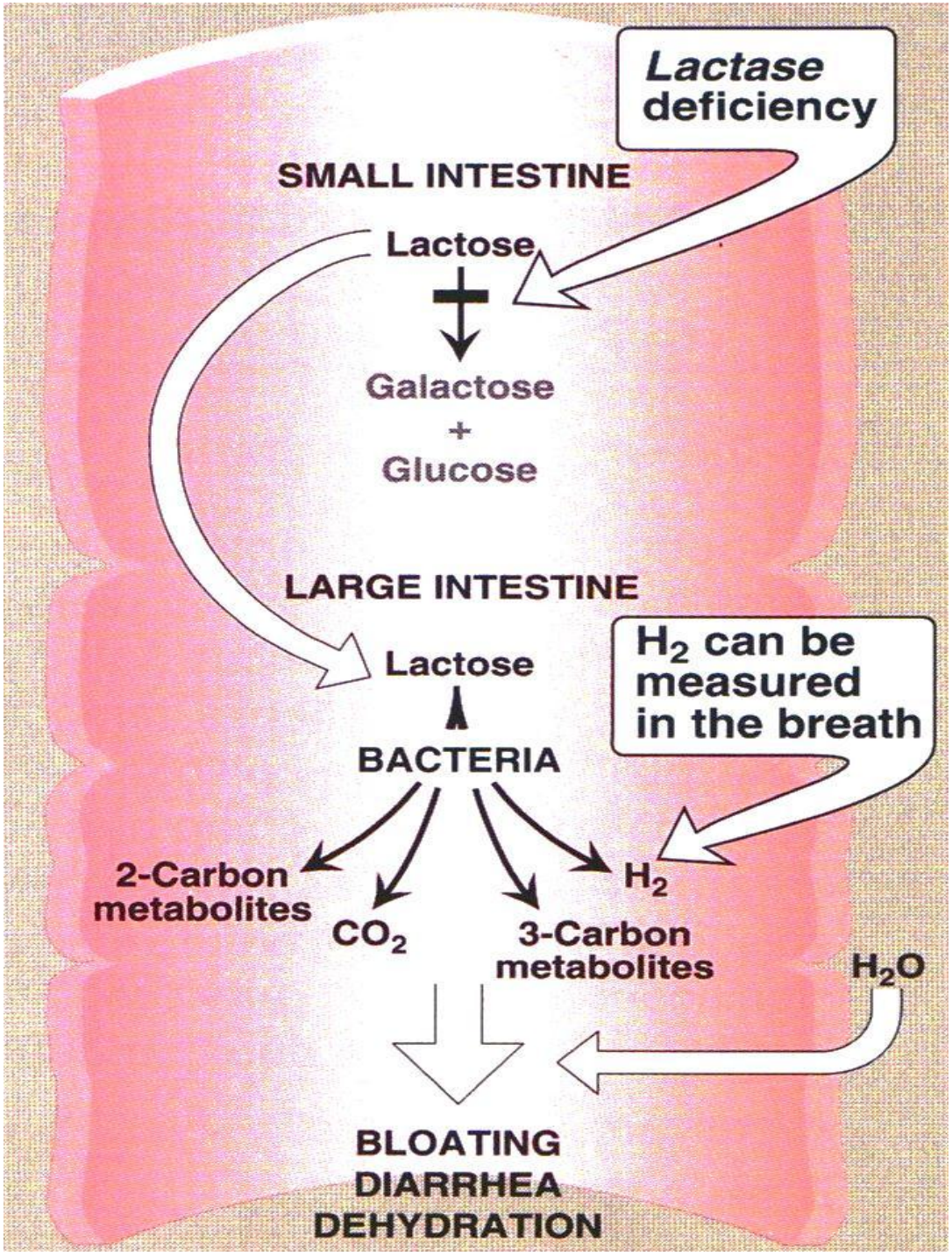

MOUTH
α-amylase
Starch dextrins
Isomaltose
Maltose
Lactose
Sucrose
Cellulose
Starch
Lactose
Sucrose
Cellulose
STOMACH
Low pH
stops action
of salivary
amylase
SMALL
INTESTINE
PANCREAS
Pancreatic
α-amylase
to
LIVER
Isomaltose
Maltose
Lactose
Sucrose
Portal
circulation
Mucosal cell
membrane-bound
enzymes:
(isomaltase
maltase
lactase
sucrase)
Glucose
Fructose
Galactose
Cellulose


Lactase deficiency
SMALL INTESTINE
Lactose
Galactose
+
Glucose
LARGE INTESTINE
Lactose
BACTERIA
H2 can be measured in the breath
2-Carbon metabolites
CO2
H2
3-Carbon metabolites
H2O
BLOATING
DIARRHEA
DEHYDRATION

Transport of Carbohydrates

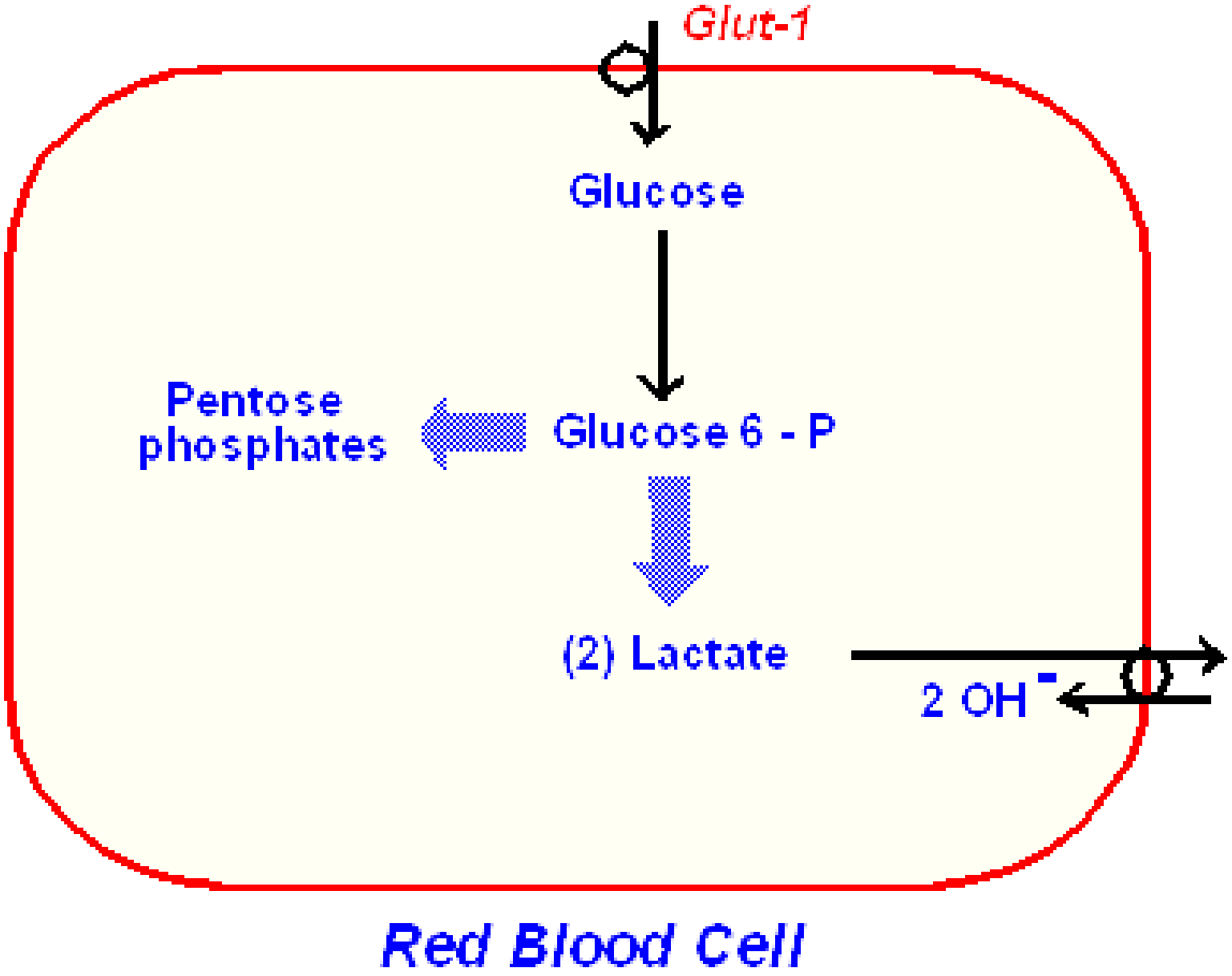
	Tissue Location	Functions
Facilitative bidirectional transporters		
GLUT 1	Brain, kidney, colon, placenta, erythrocyte	Uptake of glucose
GLUT 2	Liver, pancreatic B cell, small intestine, kidney	Rapid uptake and release of glucose
GLUT 3	Brain, kidney, placenta	Uptake of glucose
GLUT 4	Heart and skeletal muscle, adipose tissue	Insulin-stimulated uptake of glucose
GLUT 5	Small intestine	Absorption of fructose
Sodium-dependent unidirectional transporter		
SGLT 1	Small intestine and kidney	Active uptake of glucose from lumen of intestine and reabsorption of glucose in proximal tubule of kidney against a concentration gradient

Glucose Metabolism Processes

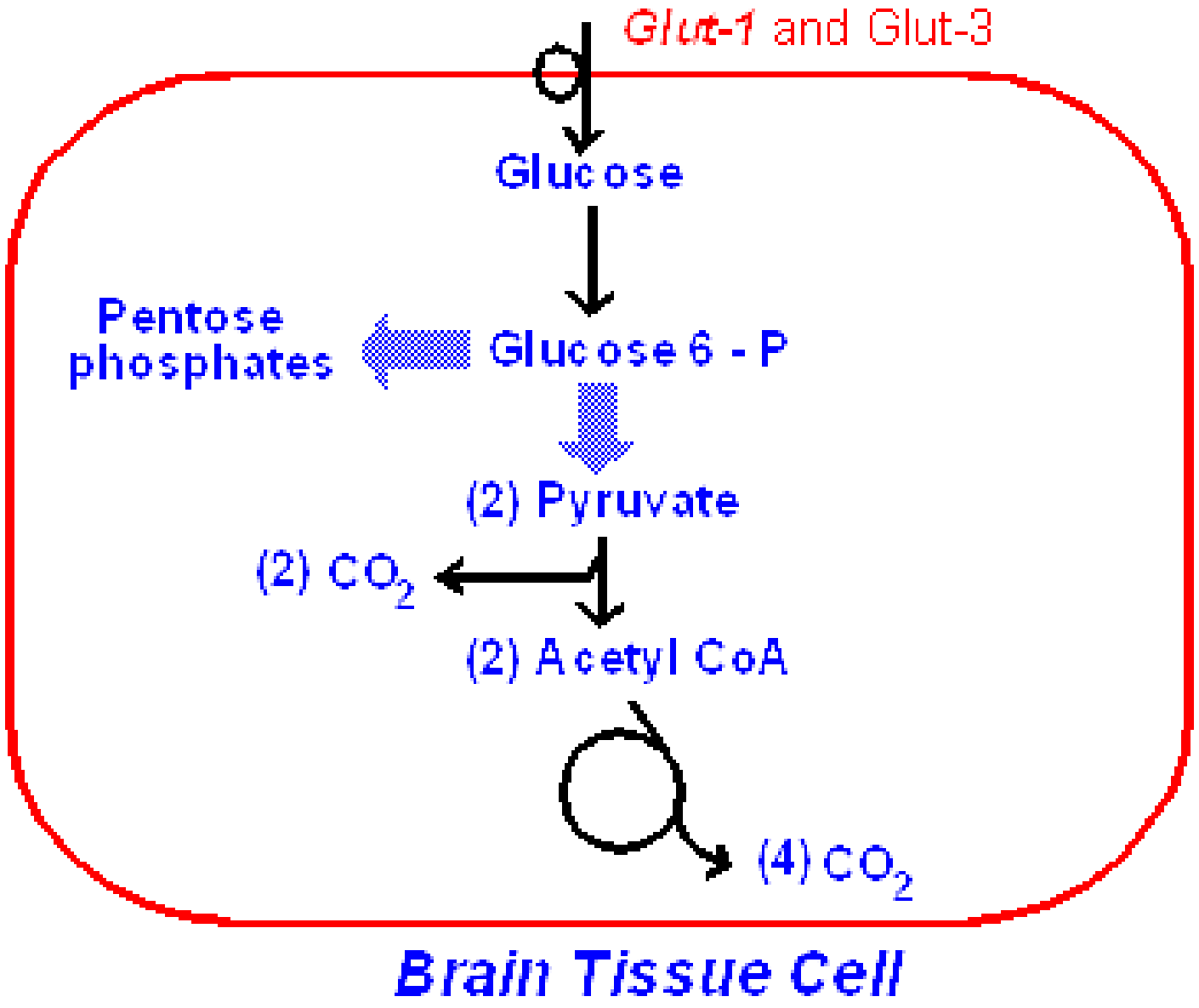
GLUCOSE METABOLISM PROCESSES	SUBSTRATE	PRODUCT	GLUCOSE METABOLISM USE
Glycolysis (Anaerobic) Anaerobic conversion of glucose to pyruvate or lactate	Glucose	Pyruvate/ lactate + ATP	Energy production (2 ATP)
Glycogenesis Process of glycogen formation from glucose	Glucose	Glycogen	Storage of glucose as glycogen in liver and muscle
Glycogenolysis Breakdown of glycogen to form glucose	Glycogen	Glucose	Release of glucose from glycogen for energy (muscle) or increase of blood glucose (liver) to maintain homeostasis
Gluconeogenesis Formation of glucose from noncarbohydrate sources (proteins, lipids)	Amino acids Lactate Glycerol	Glucose	Increase of blood glucose (liver) when glycogen stores are depleted
TCA (Tricarboxylic Acid) Cycle and Electron Transport System Aerobic phase of glucose metabolism within the mitochondria of the cell	Pyruvate → acetyl CoA	ATP	Energy production (24 ATP, 12 per acetyl CoA molecule)
Hexose Monophosphate Pathway (HMP) Alternate pathway for glucose oxidation	Glucose	NADPH	Energy source for many anabolic reactions and glycolysis in RBCs, since they lack mitochondria

NADPH, reduced form of nicotinamide adenine dinucleotide phosphate; RBCs, red blood cells.

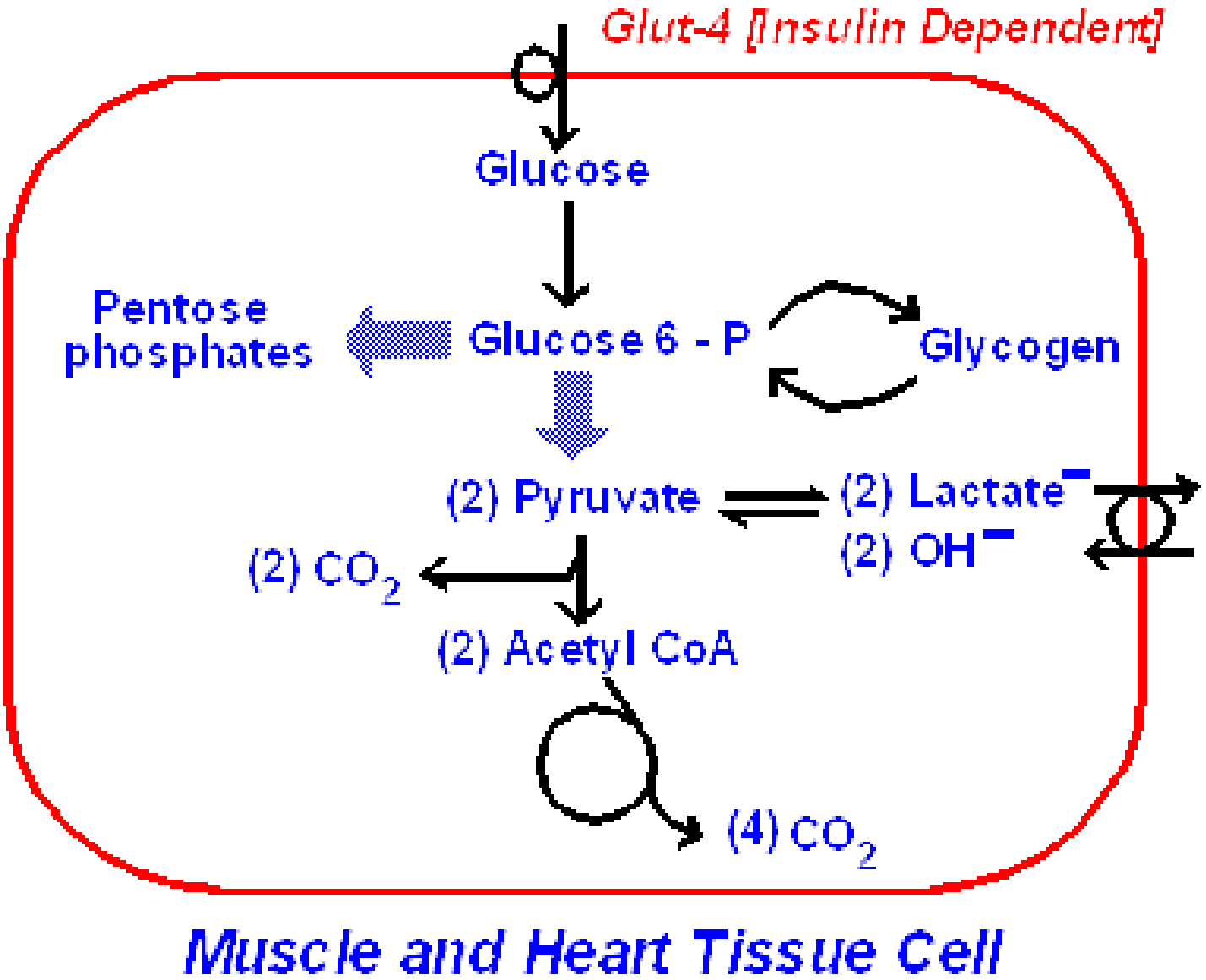
Tissue's Metabolism of Glucose



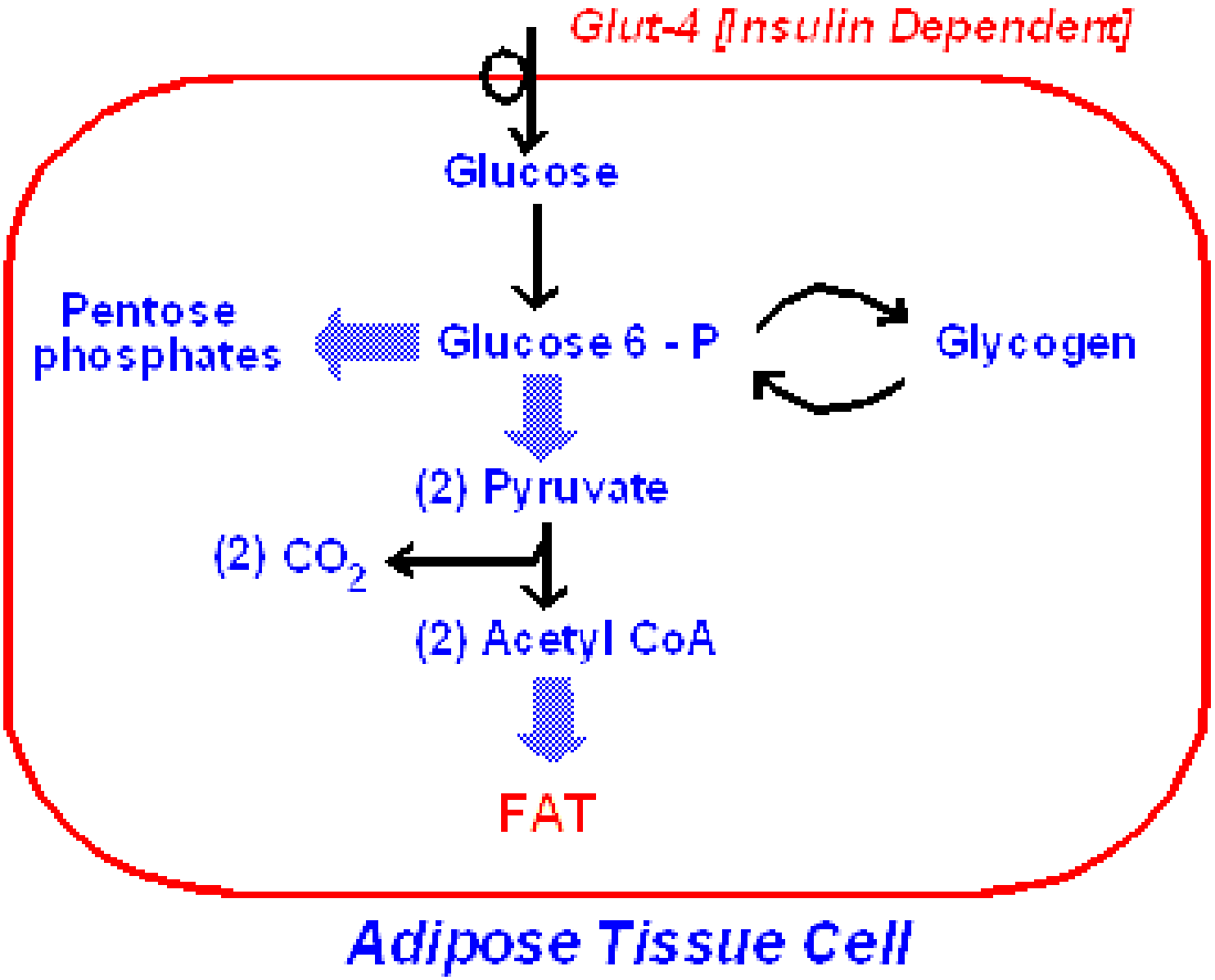
Tissue's Metabolism of Glucose



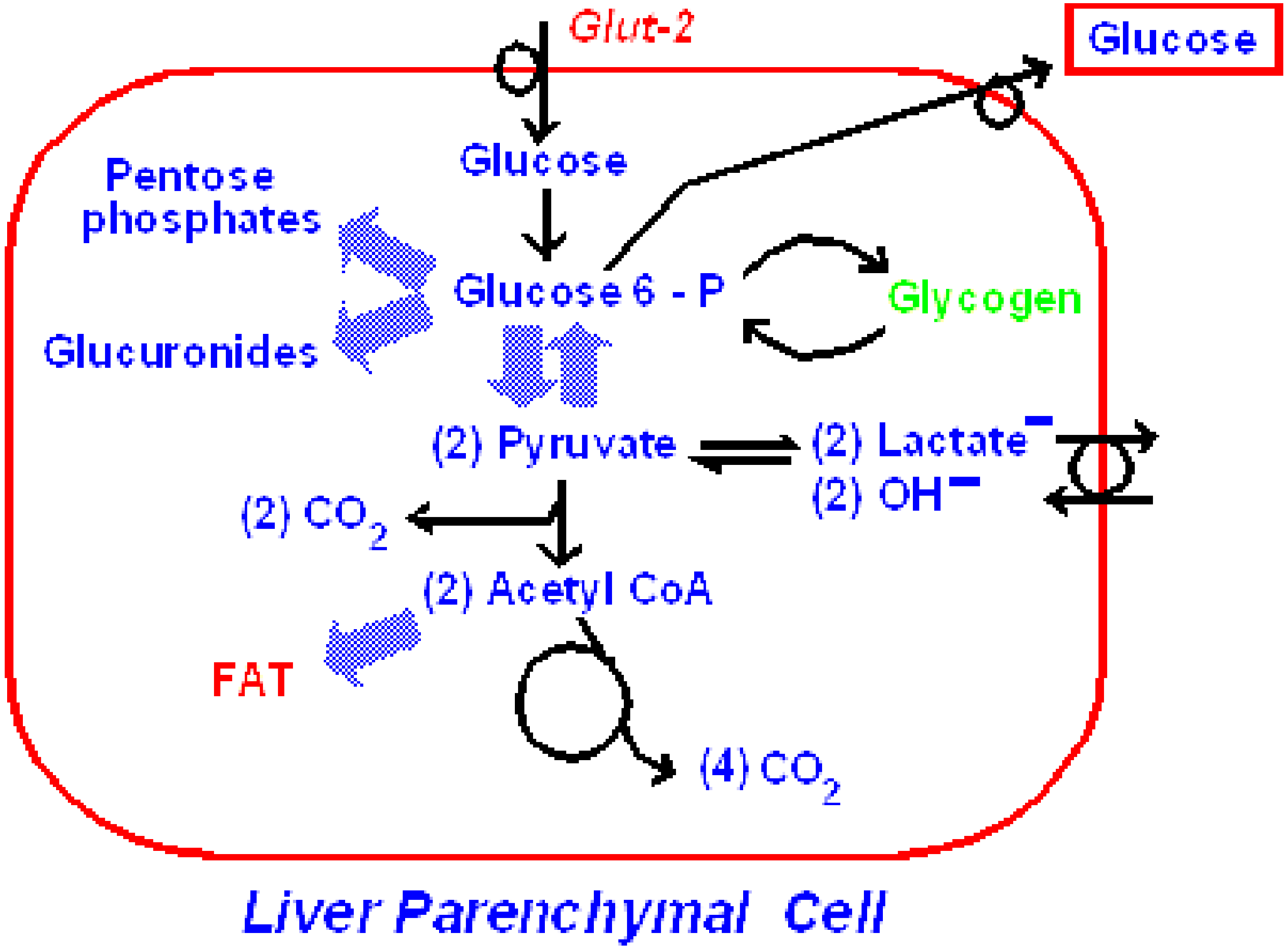
Tissue's Metabolism of Glucose

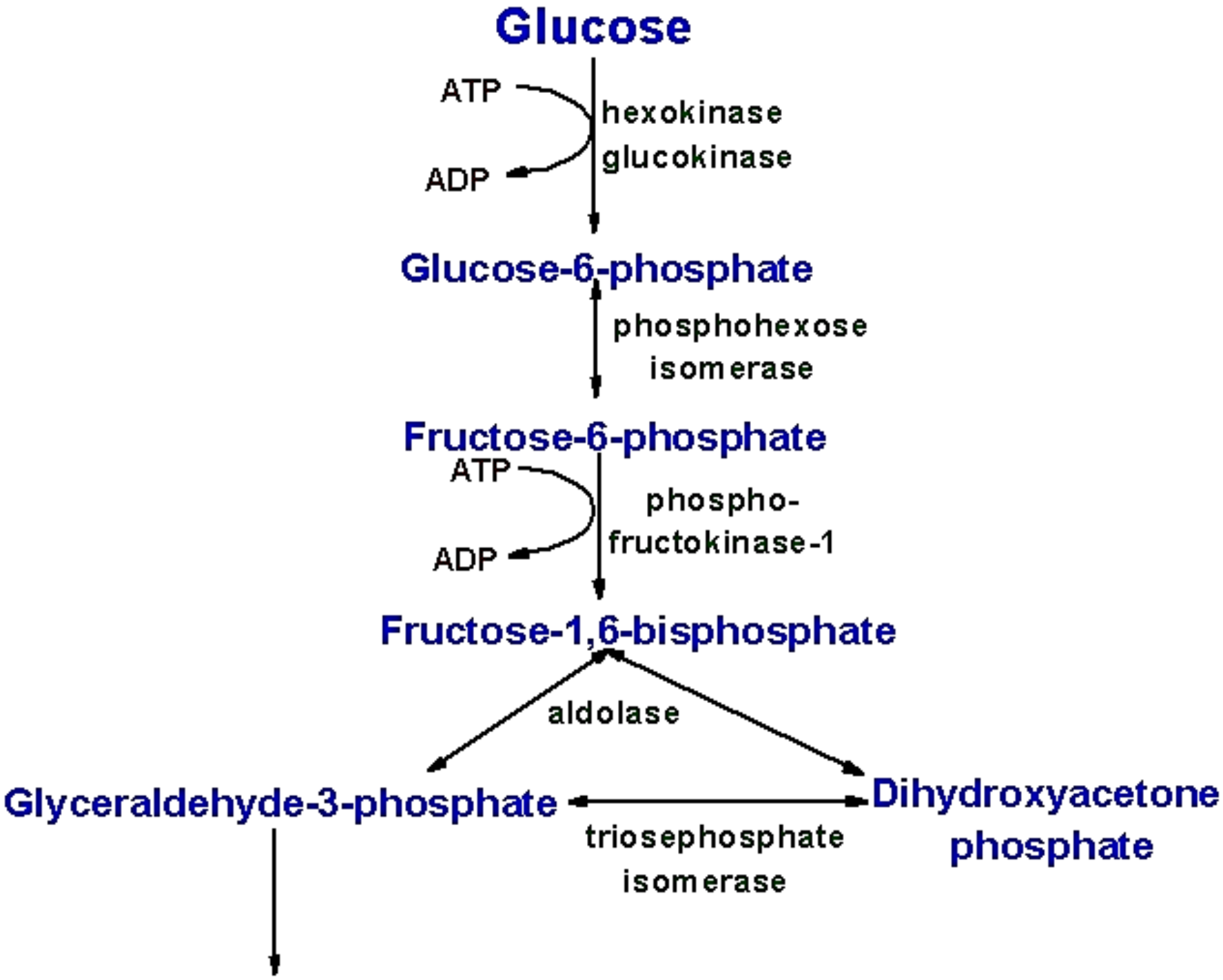


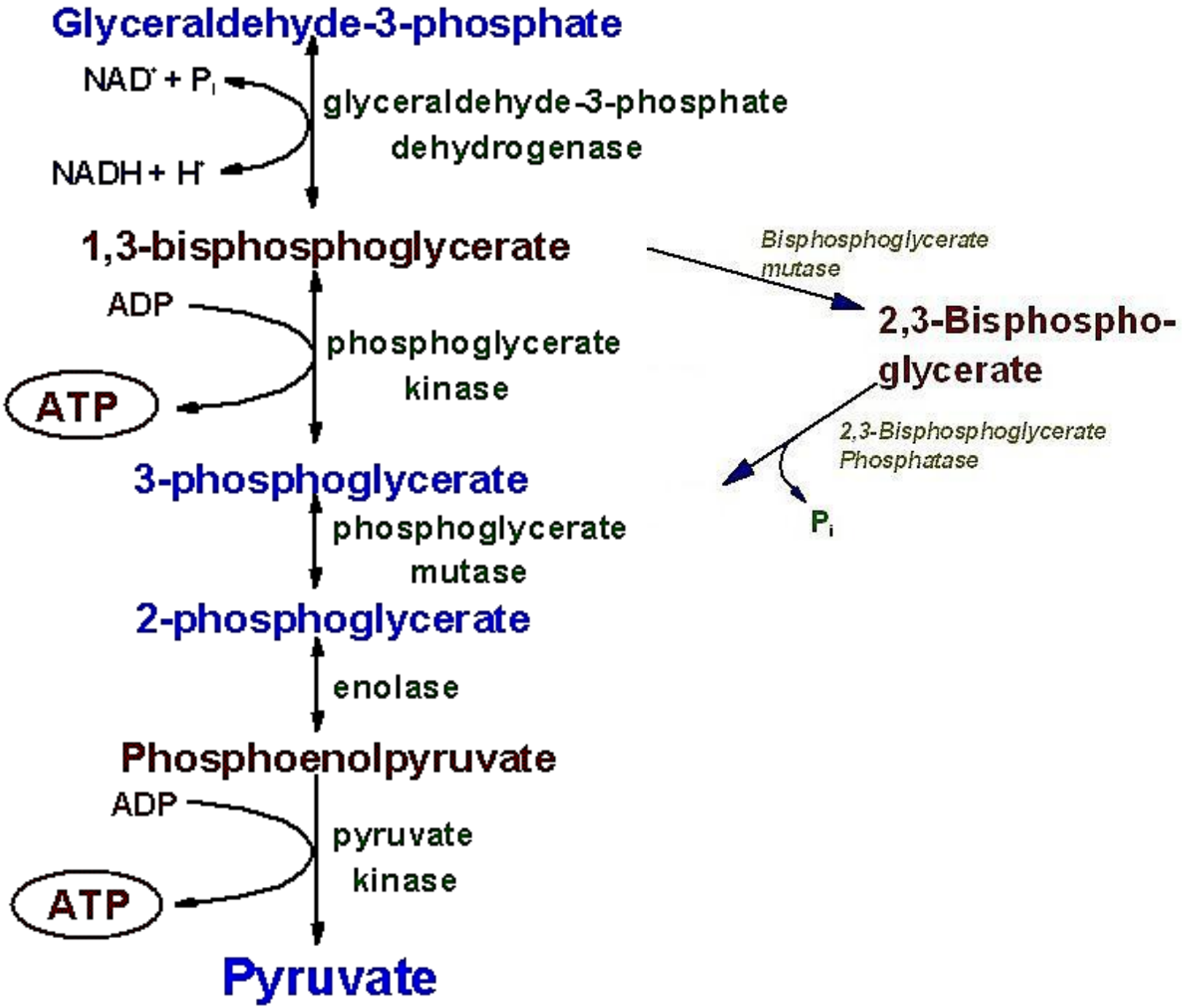
Tissue's Metabolism of Glucose



Tissue's Metabolism of Glucose




Glucose
ATP
ADP
hexokinase
glucokinase
Glucose-6-phosphate
phosphohexose
isomerase
Fructose-6-phosphate
ATP
ADP
phospho-
fructokinase-1
Fructose-1,6-bisphosphate
aldolase
Glyceraldehyde-3-phosphate
triosephosphate
isomerase
Dihydroxyacetone
phosphate


Glyceraldehyde-3-phosphate
NAD+ + Pi
NADH + H+
glyceraldehyde-3-phosphate dehydrogenase
1,3-bisphosphoglycerate
Bisphosphoglycerate mutase
2,3-Bisphospho-glycerate
ADP
ATP
phosphoglycerate kinase
2,3-Bisphosphoglycerate Phosphatase
Pi
3-phosphoglycerate
phosphoglycerate mutase
2-phosphoglycerate
enolase
Phosphoenolpyruvate
ADP
ATP
pyruvate kinase
Pyruvate

Chemical Inhibitors of Glycolysis

Fluoride, F^-

Fluoride ion is a potent inhibitor of Enolase, it is believed to form a complex with magnesium and inorganic phosphate which interferes with the interaction of the enzyme with substrate *

* ***fluoride has many other effects on the body, some of which are toxic and some of which may be beneficial (i.e., hardening of dental enamel***

Arsenate

Arsenate is a phosphate analog and will form and arsenoanalog of 1,3 bisphosphoglycerate, 1-arsenato 3-phosphoglycerate which spontaneously hydrolyses and prevents the formation of both 1,3 bisphosphoglycerate and ATP in the mitochondrion.

* ***arsenate will not only shut down glycolysis but also interfere with oxidative phosphorylation and starve the cell for high-energy equivalents***

Fates of Pyruvate under Anaerobic Condition

Lactate fermentation

Lactate

Produced by muscles when the body can't supply enough O_2.

pyruvate → lactate

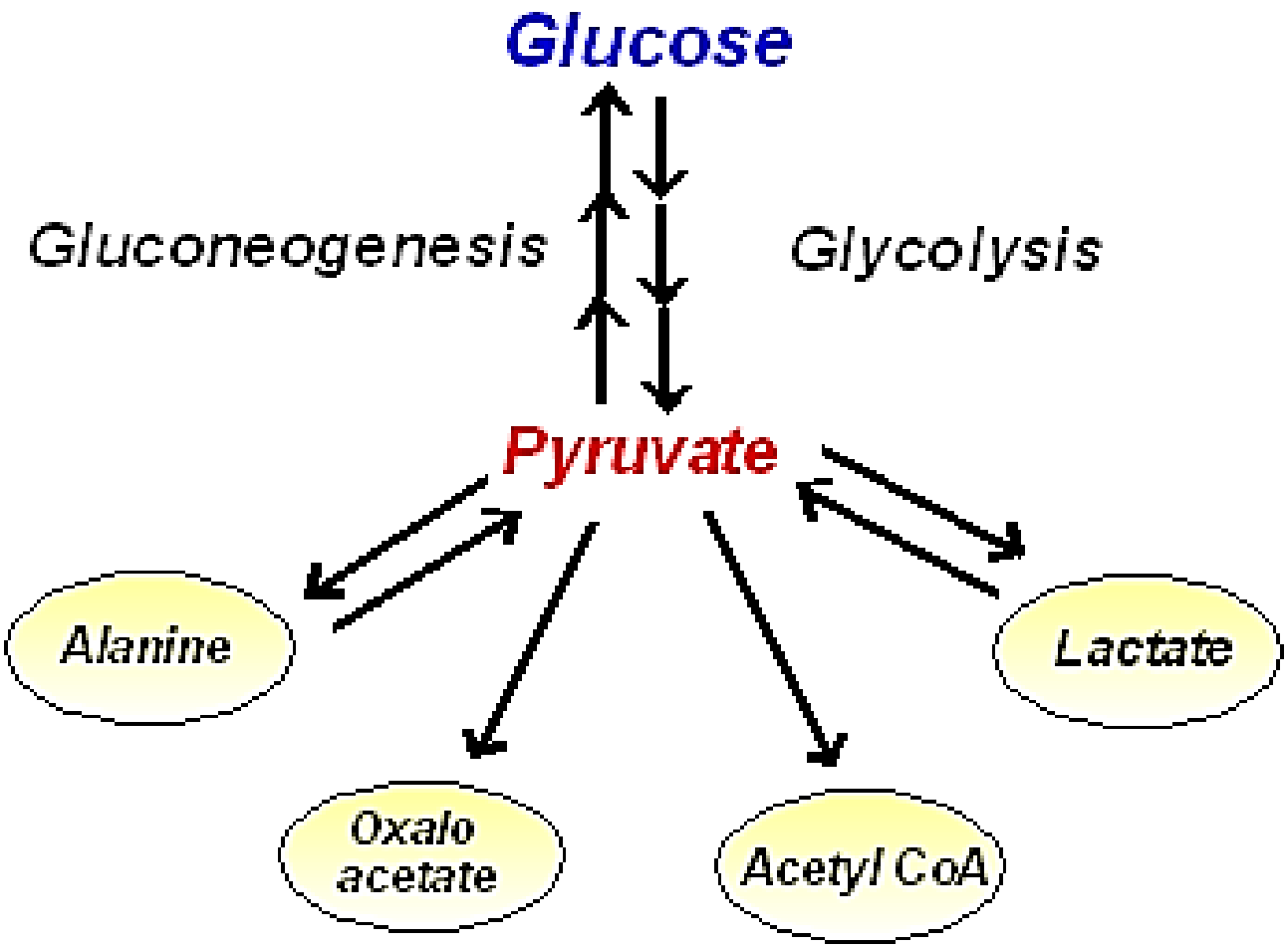
NADH → NAD^+

Anaerobic conversion of pyruvate to lactate permits regeneration of NAD^+.

Body can then make more ATP - at a cost. Creates an oxygen debt.

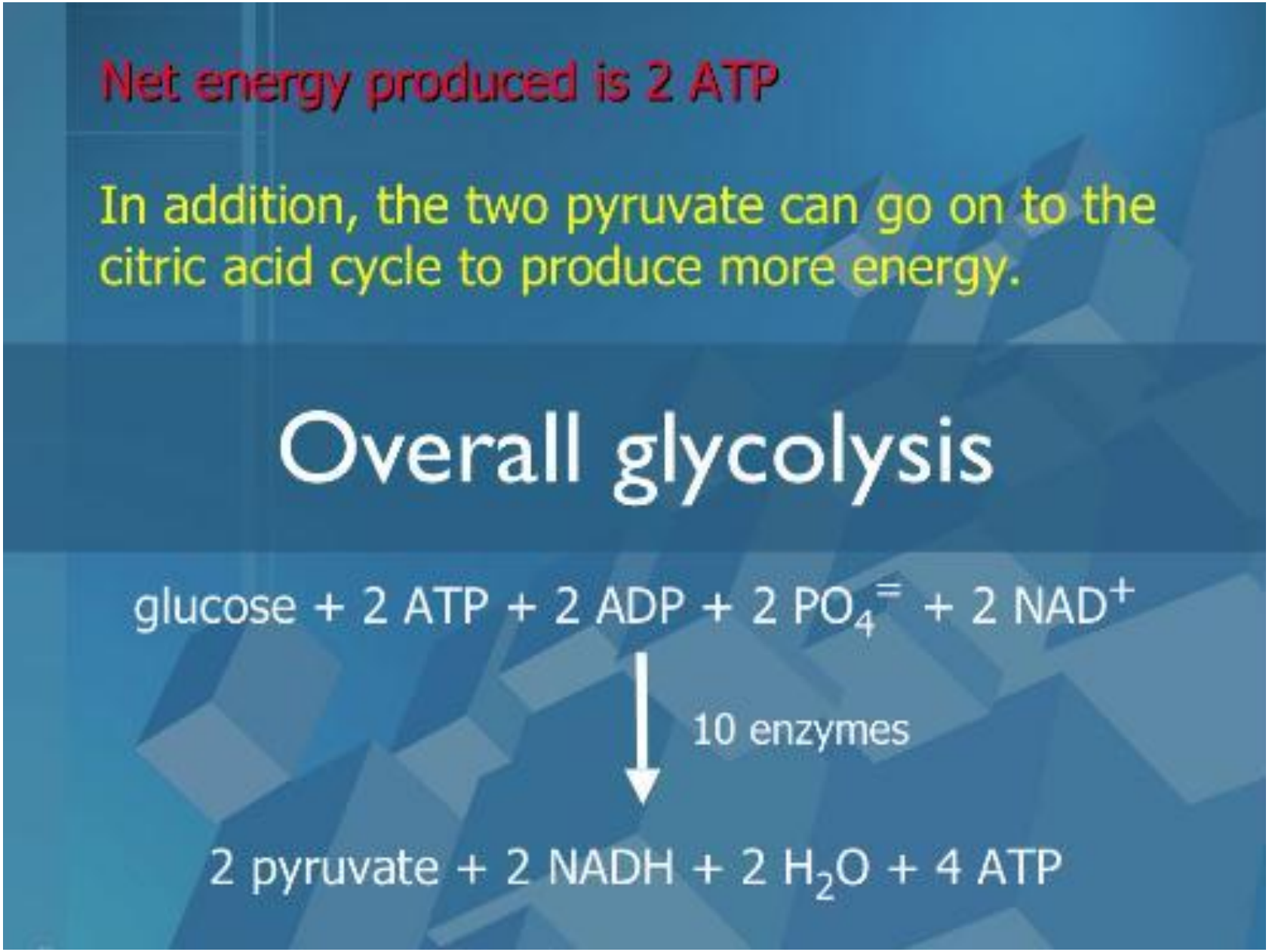
Must use extra O_2 to oxidize lactate later

Fates of Pyruvate under Aerobic Condition



Pyruvate has several origins and metabolic fates

Energy Yield of Glycolysis (Aerobic & Anaerobic)



Shuttle Systems May Produce Different ATP Yields

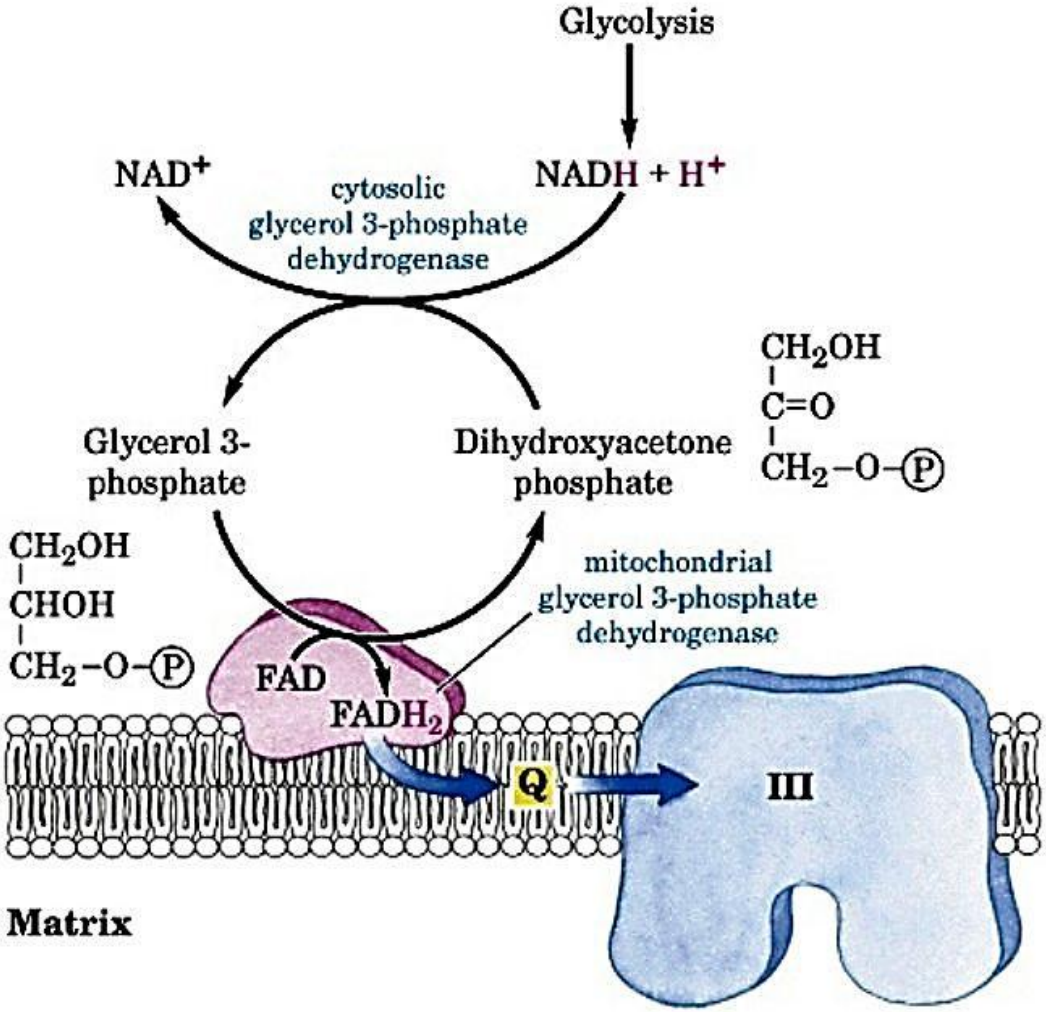
Glycerol Phosphate Shuttle Yields $FADH_2$

This results in the potential for the synthesis of 1.5 - 2 ATP through mitochondrial oxidative phosphorylation

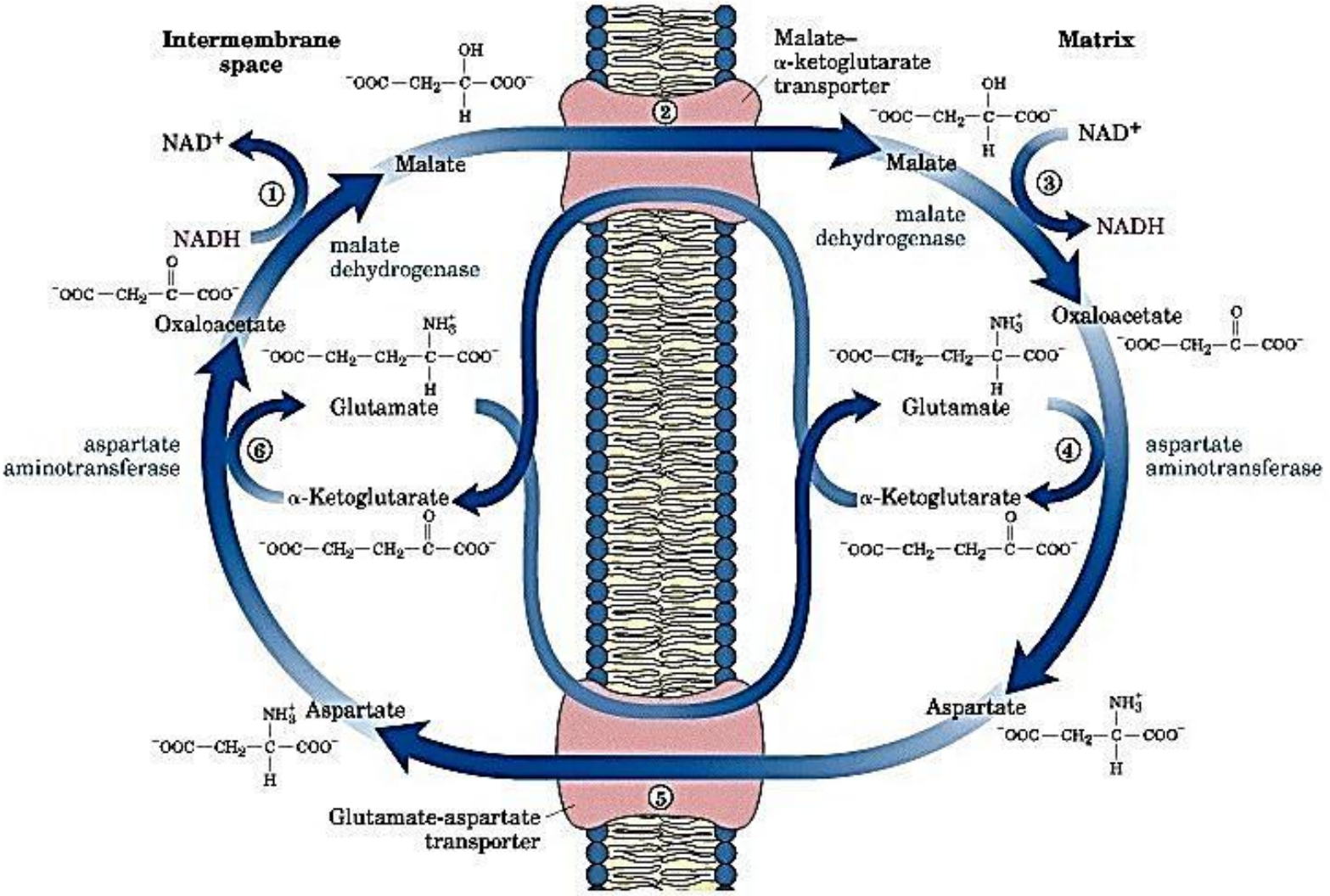
Malate - aspartate Shuttle Yields NADH

This results in the potential for the synthesis of 2.5 - 3 ATP through mitochondrial oxidative phosphorylation

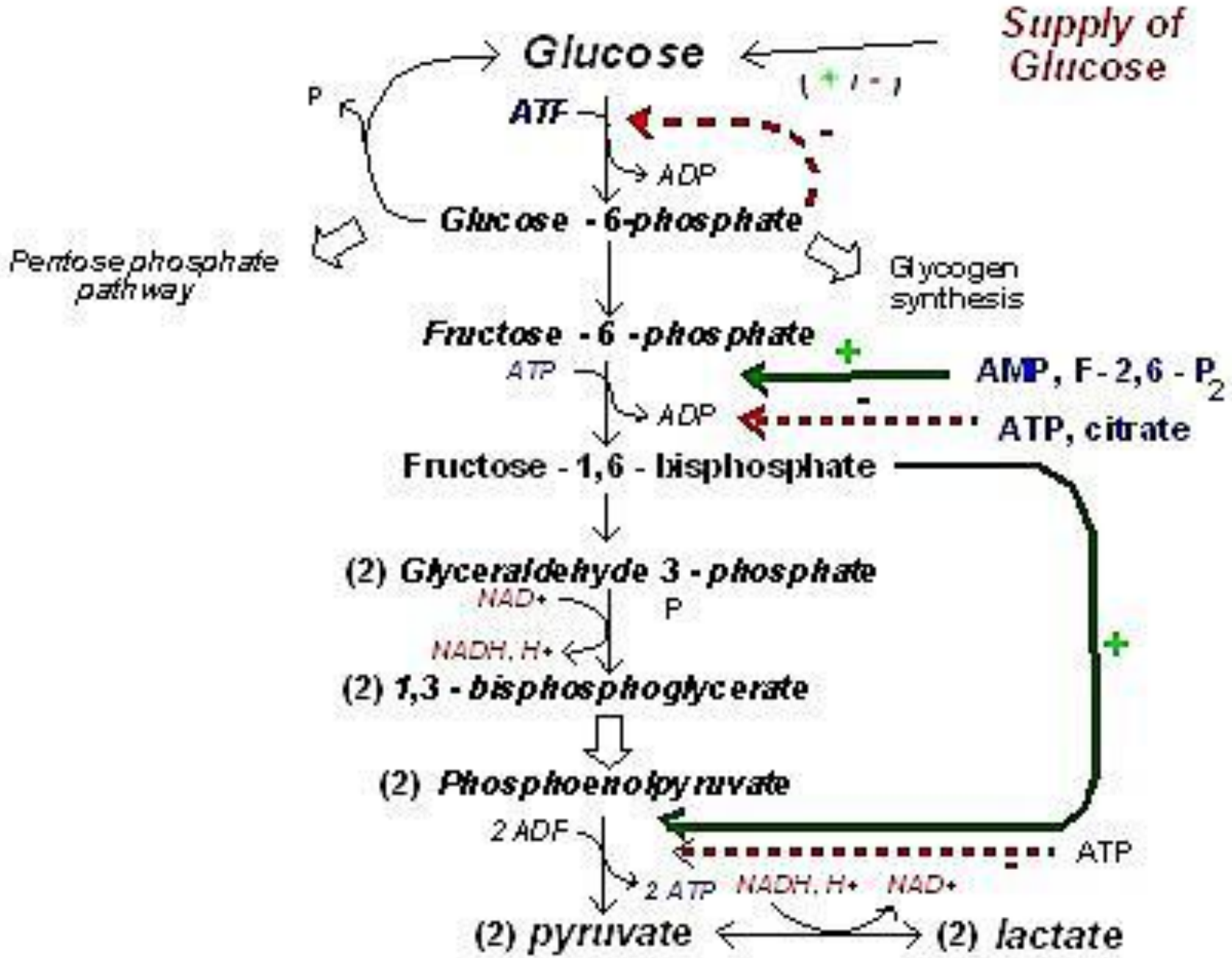
In muscle and brain, the glycerol-P shuttle brings cytoplasmic NADH to the ETS



Malate-aspartate shuttle



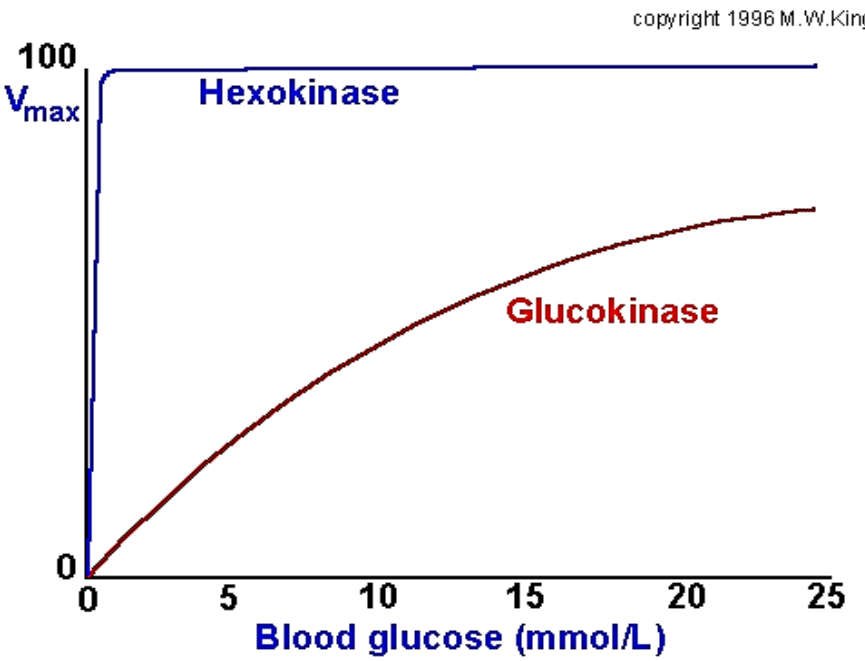
Lori Lafargue Photography

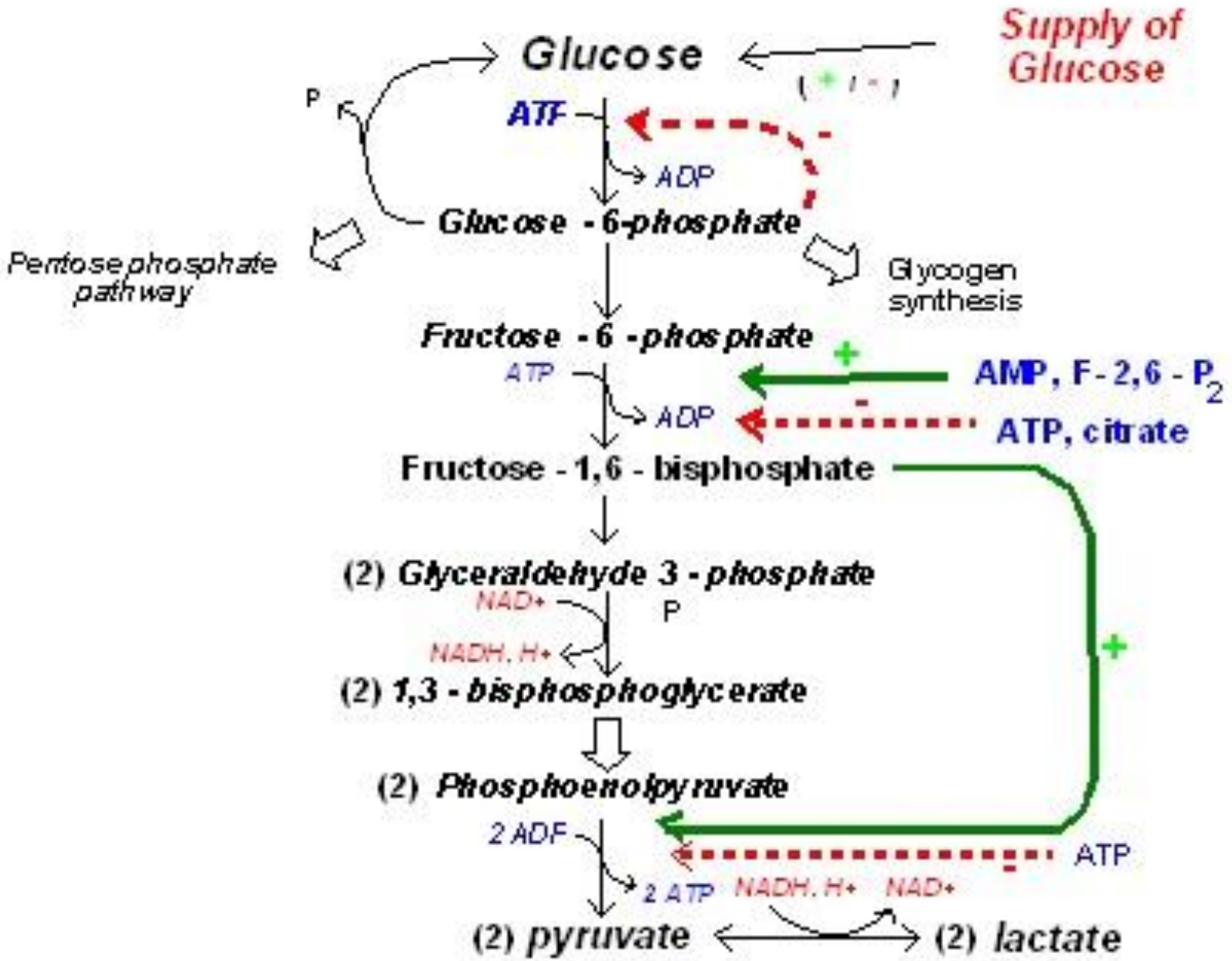

Supply of Glucose
Glucose
(+ / -)
P
ATP
ADP
Glucose - 6-phosphate
Pentose phosphate pathway
Glycogen synthesis
Fructose - 6 -phosphate
ATP
ADP
+
AMP, F-2,6 - P2
-
ATP, citrate
Fructose - 1,6 - bisphosphate
(2) Glyceraldehyde 3 - phosphate
NAD+
P
NADH, H+
(2) 1,3 - bisphosphoglycerate
(2) Phosphoenolpyruvate
2 ADP
2 ATP
ATP
NADH, H+
NAD+
(2) pyruvate
(2) lactate

Glycolysis (HK Regulation)

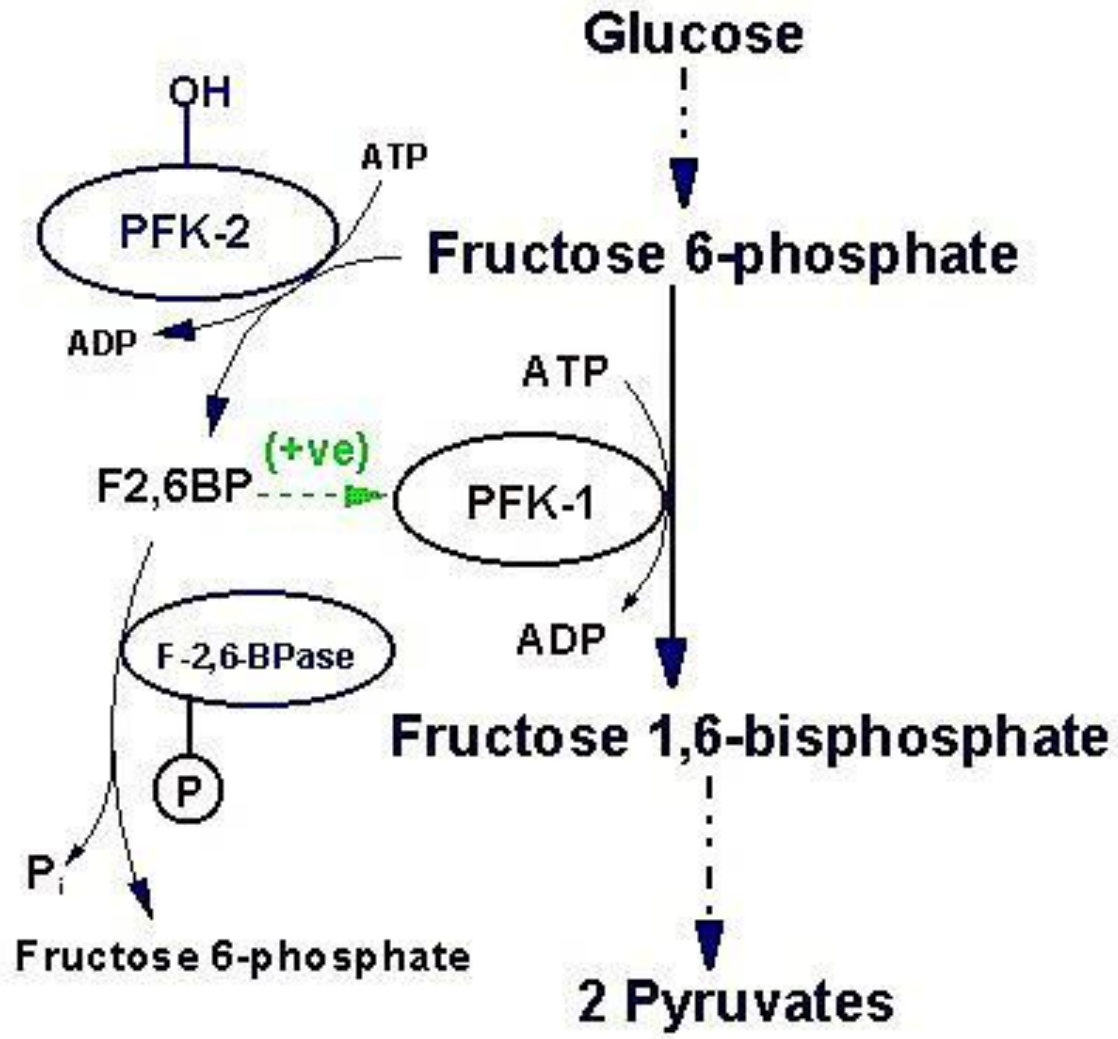
	Hexokinase (muscle, etc.)	*Glucokinase** (liver)
Km	low	high
Vmax	similar	similar
Inhibition by G-6-P	yes	no

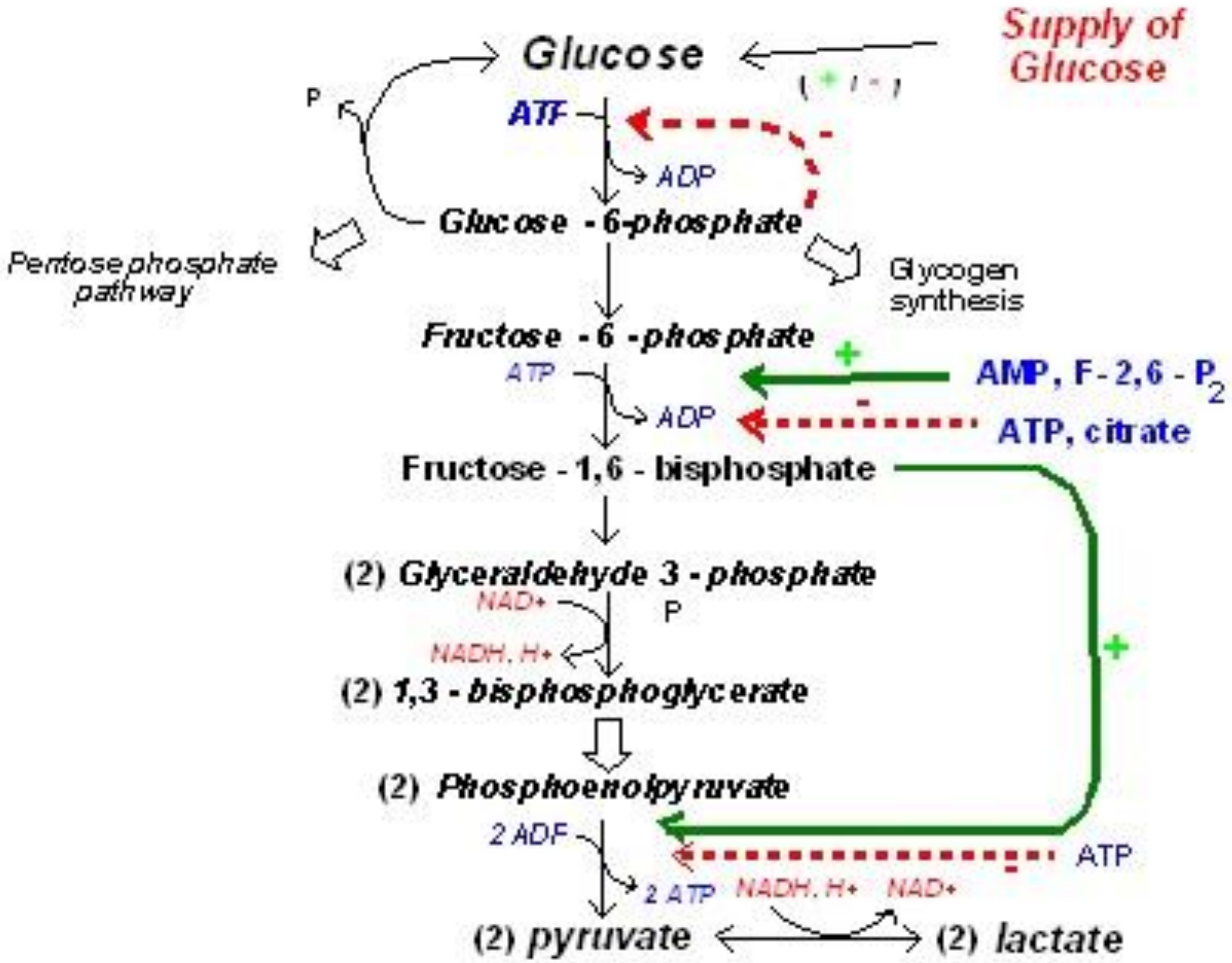
* [Insulin Dependent]



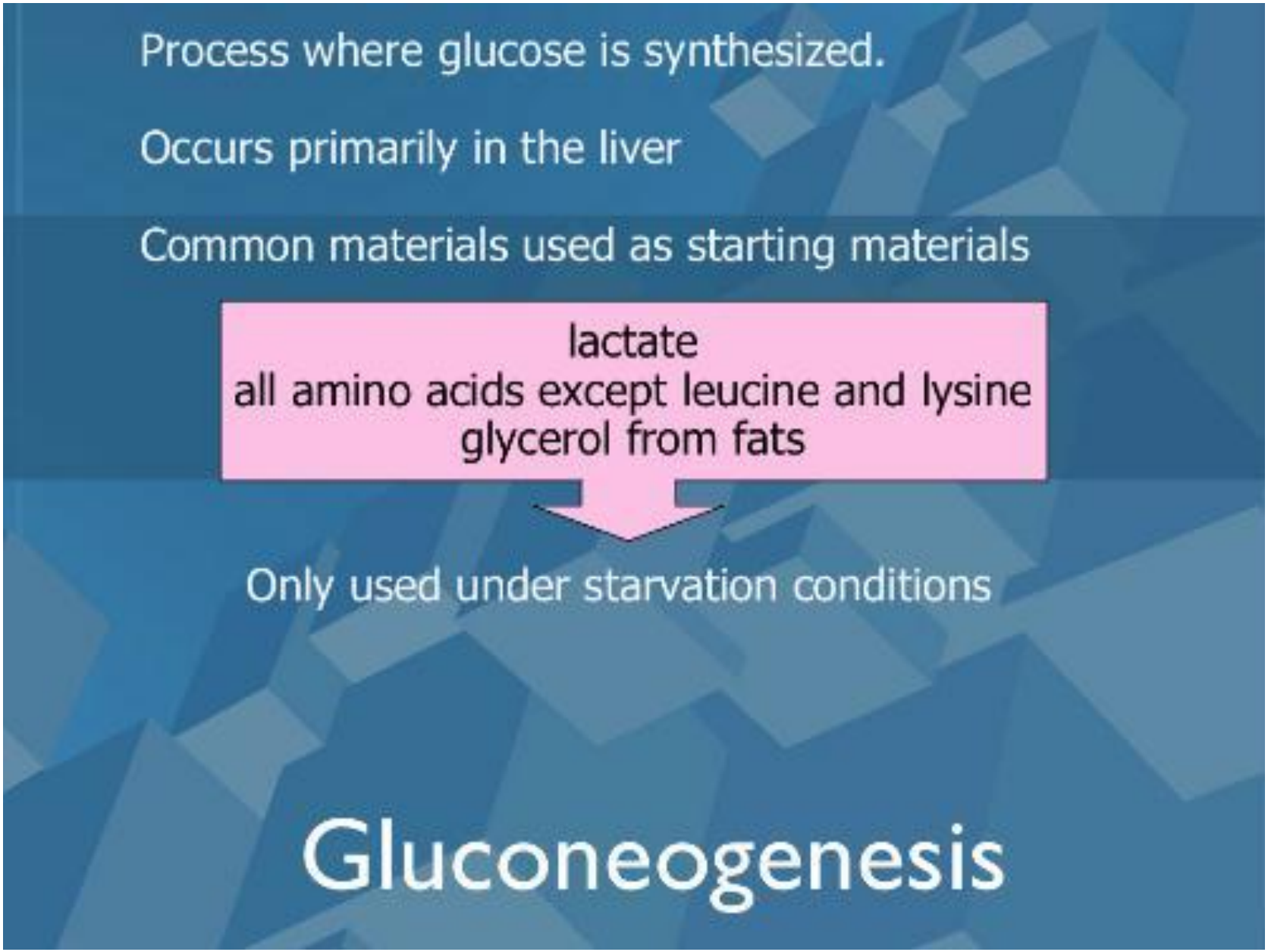

Supply of Glucose
Glucose
P
ATP
ADP
Glucose - 6-phosphate
Pentose phosphate pathway
Glycogen synthesis
Fructose - 6 -phosphate
ATP
ADP
AMP, F - 2,6 - P2
ATP, citrate
Fructose - 1,6 - bisphosphate
(2) Glyceraldehyde 3 - phosphate
NAD+
P
NADH, H+
(2) 1,3 - bisphosphoglycerate
(2) Phosphoenolpyruvate
2 ADP
2 ATP
ATP
NADH, H+
NAD+
(2) pyruvate
(2) lactate

Glycolysis (PFK Regulation)

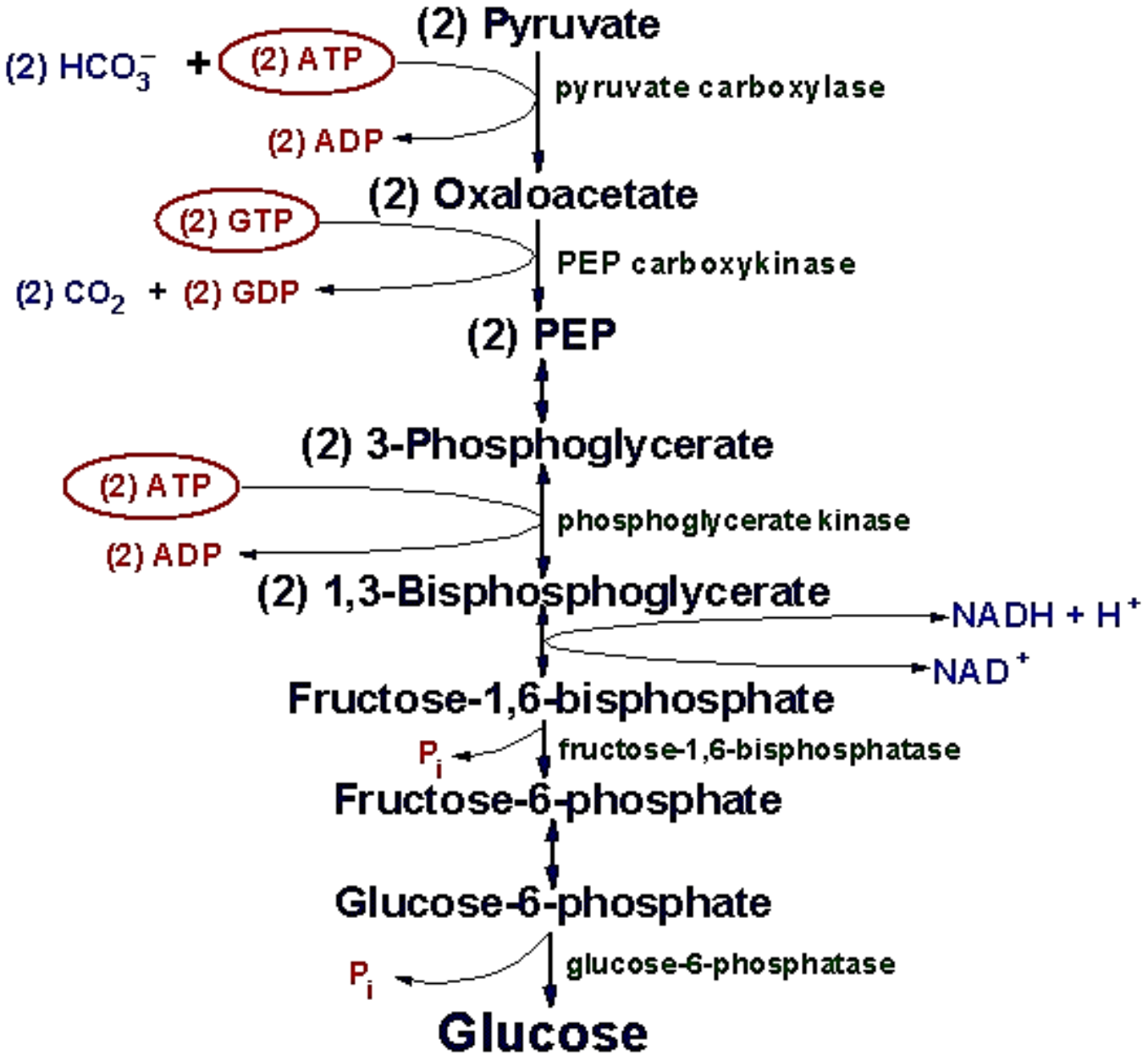



Supply of Glucose
Glucose
(+ / -)
P
ATP
ADP
Glucose - 6-phosphate
Pentose phosphate pathway
Glycogen synthesis
Fructose - 6 -phosphate
ATP
ADP
+
AMP, F-2,6 - P2
-
ATP, citrate
Fructose - 1,6 - bisphosphate
(2) Glyceraldehyde 3 - phosphate
NAD+
P
NADH, H+
(2) 1,3 - bisphosphoglycerate
(2) Phosphoenolpyruvate
2 ADP
2 ATP
ATP
NADH, H+
NAD+
(2) pyruvate
(2) lactate

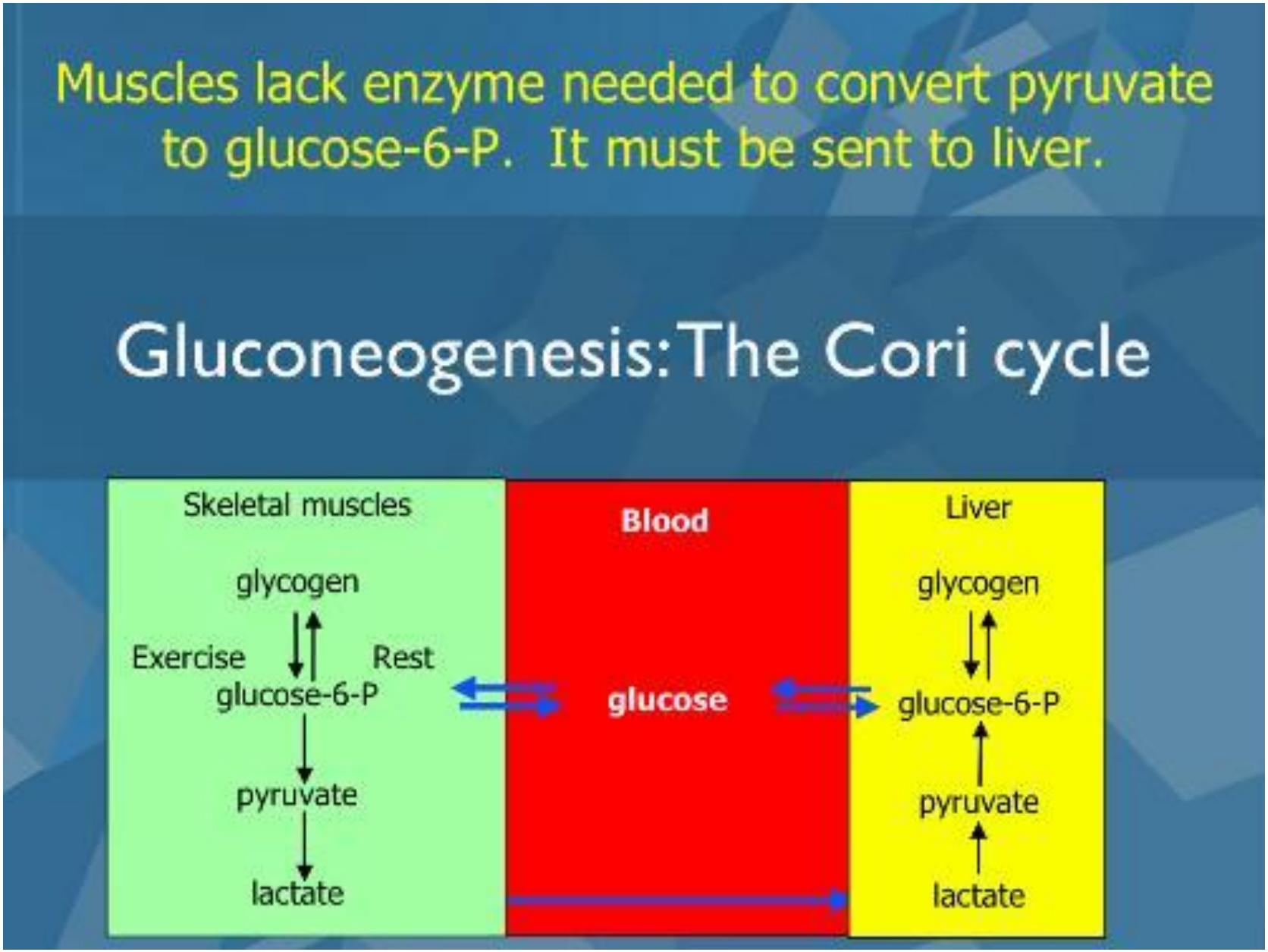
Gluconeogenesis



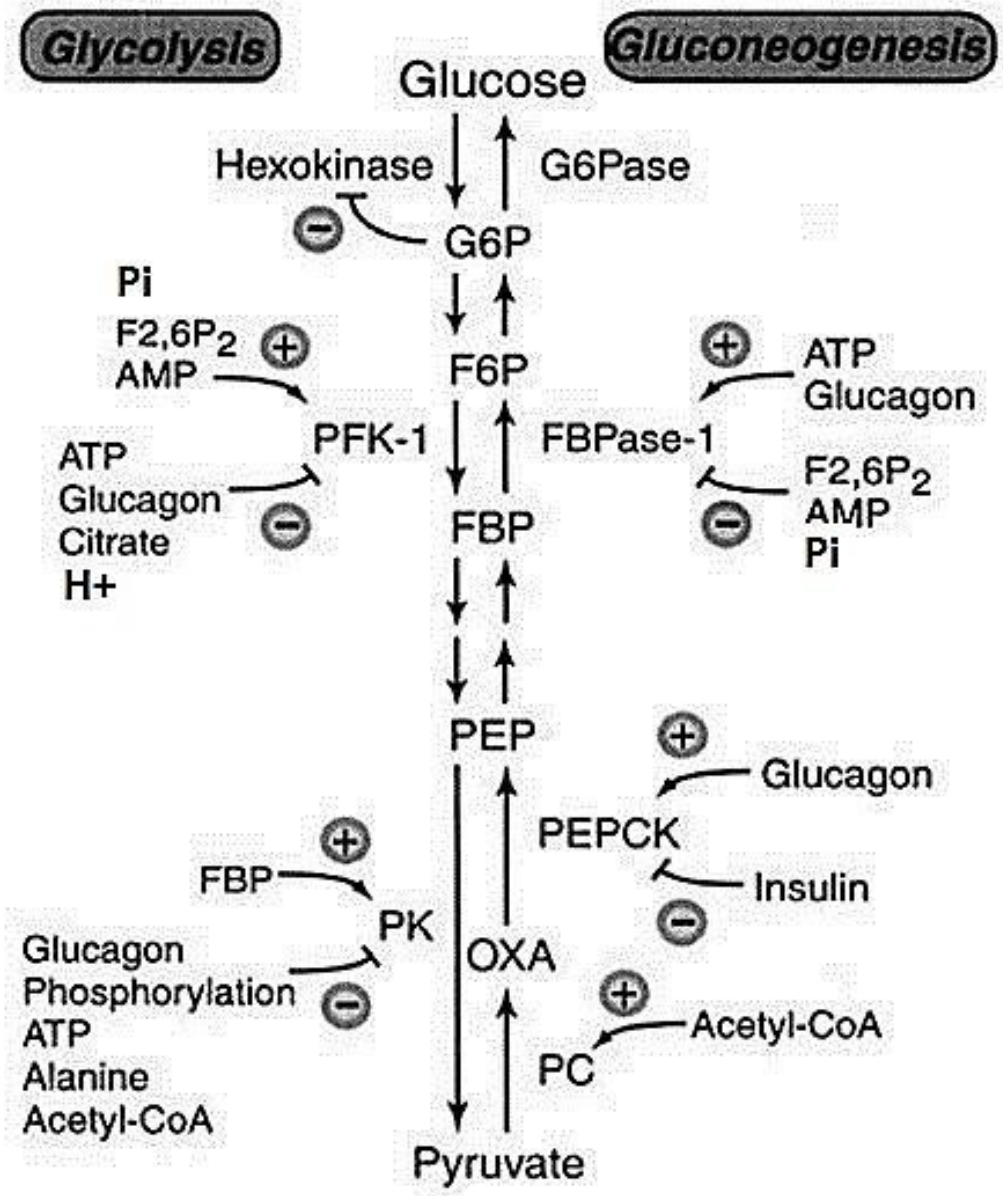
Gluconeogenesis



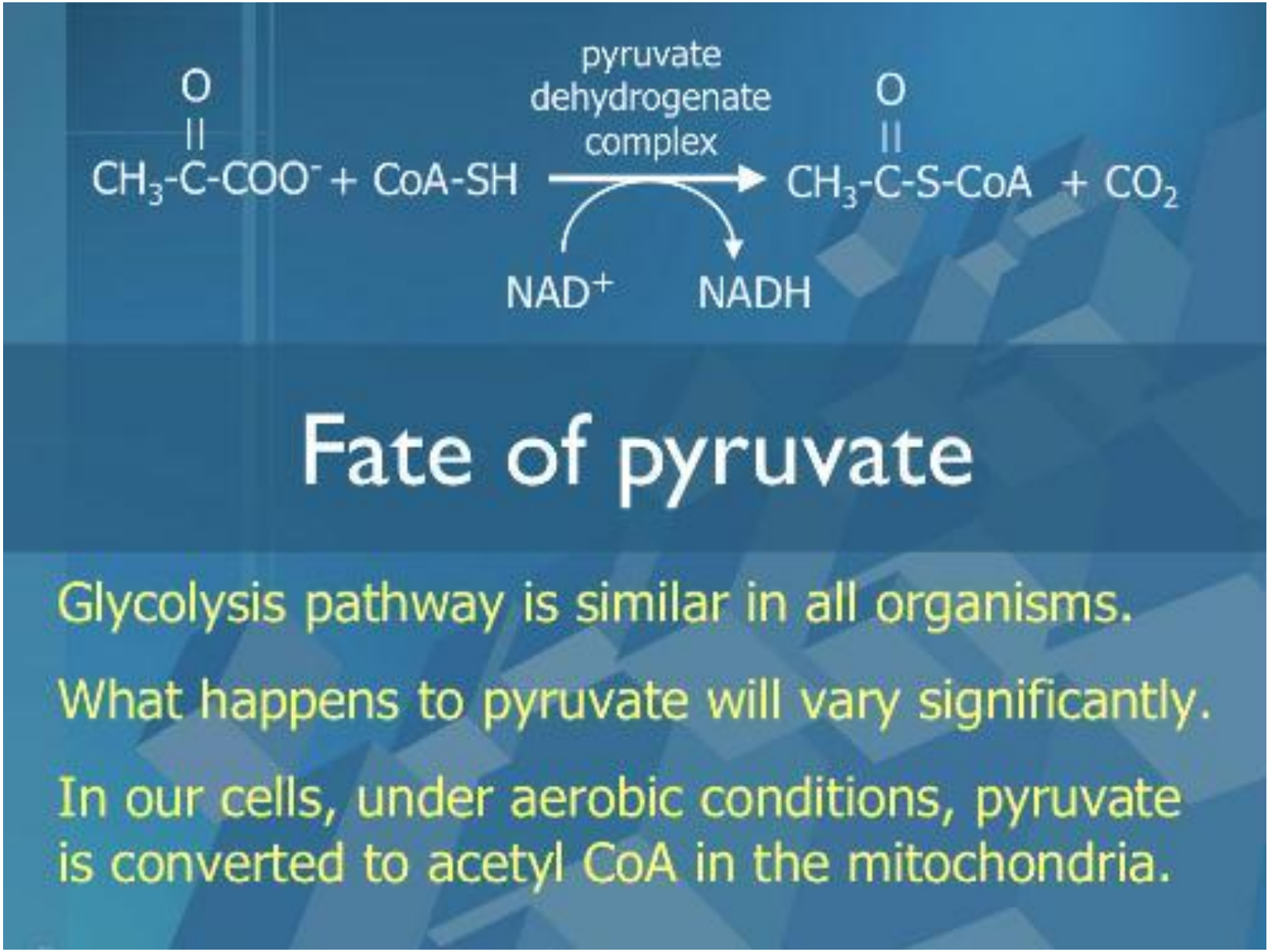
Gluconeogenesis



Control of Gluconeogenesis



Fates of Pyruvate under Aerobic Condition



The Pyruvate Dehydrogenase Reaction

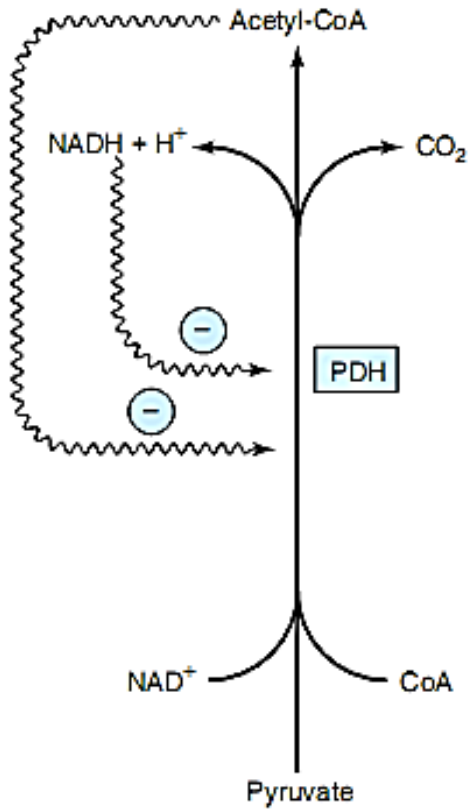
This is an irreversible reaction

This reaction is catalyzed by a multifunctional enzyme complex which requires 5 different coenzymes or cofactors and catalyzes three discrete reactions.

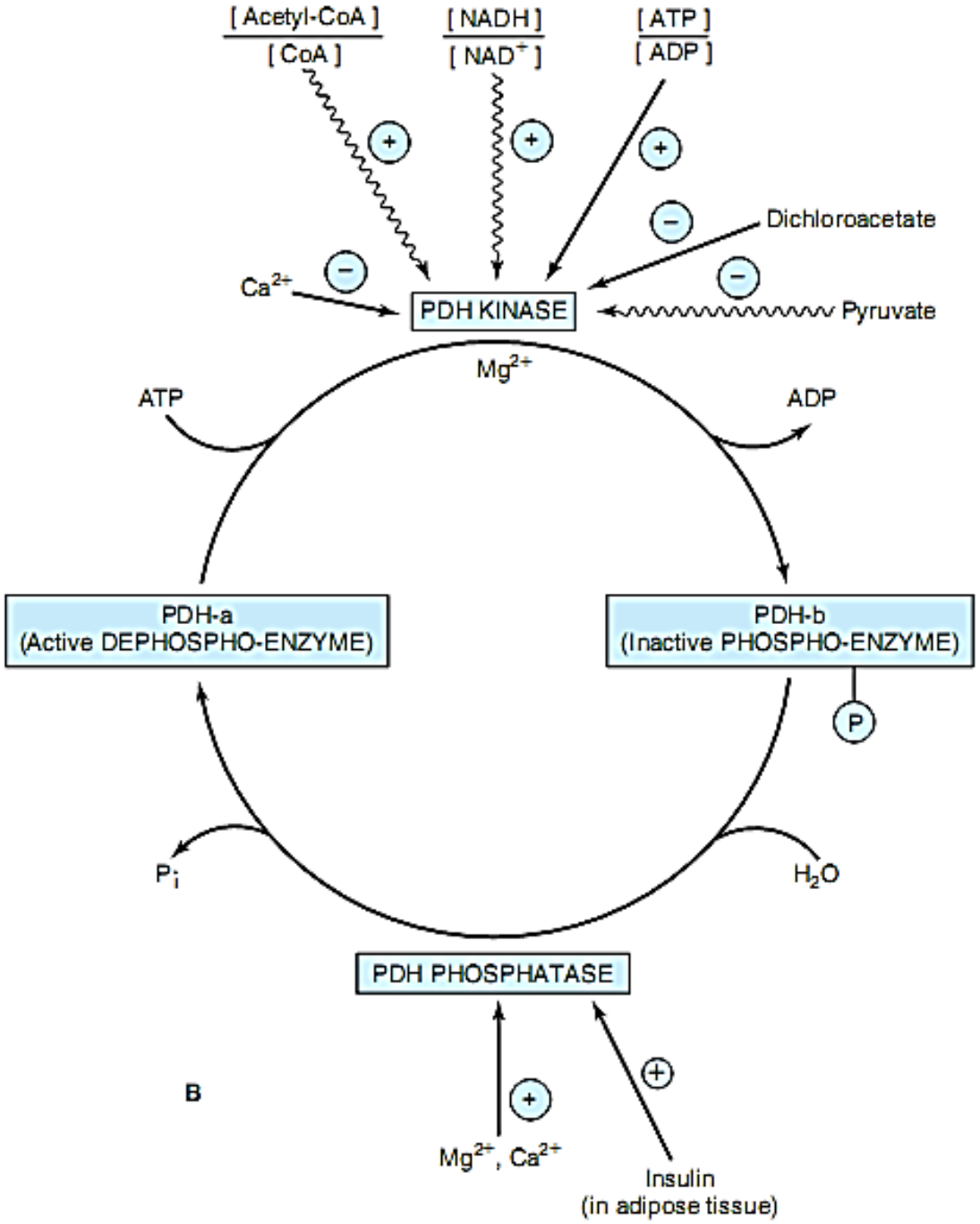
1. *component E1 (a decarboxylase)*
2. *dihydrolipoyl transacetylase (E2)*
3. *dihydrolipoyl dehydrogenase (E3)*

Pyruvate dehydrogenase complex (mitochondrion)

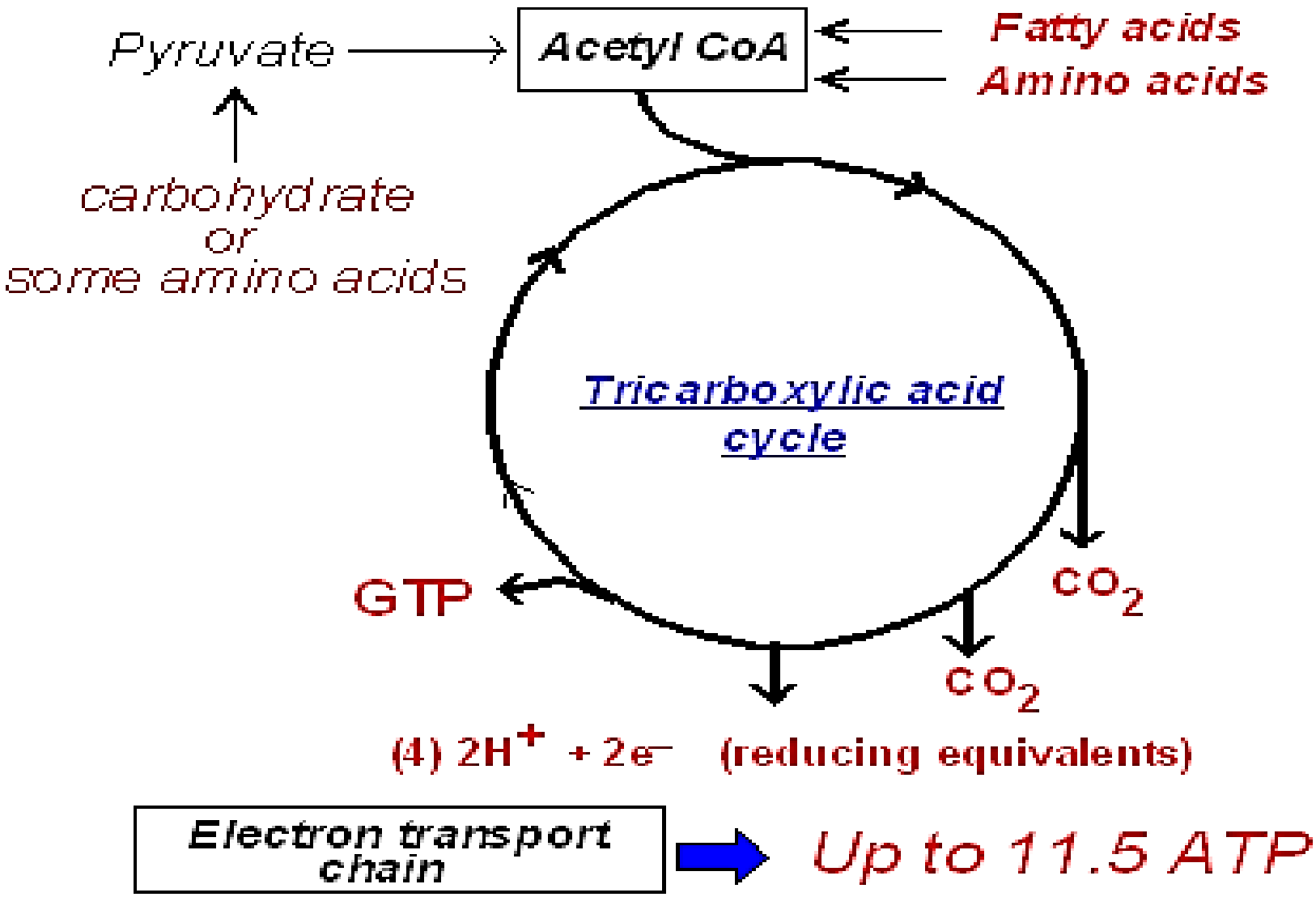
A covalent intermediate is formed with the release of CO_2 and ultimately the two remaining carbons are transferred to CoASH to form acetyl CoA and regenerate the enzyme. This is a highly regulated enzyme. The 5 cofactors or coenzymes involved are NADH, Thiamin pyrophosphate, lipoic acid, FAD and CoASH. This is a key enzyme in metabolism and on EXAMS.

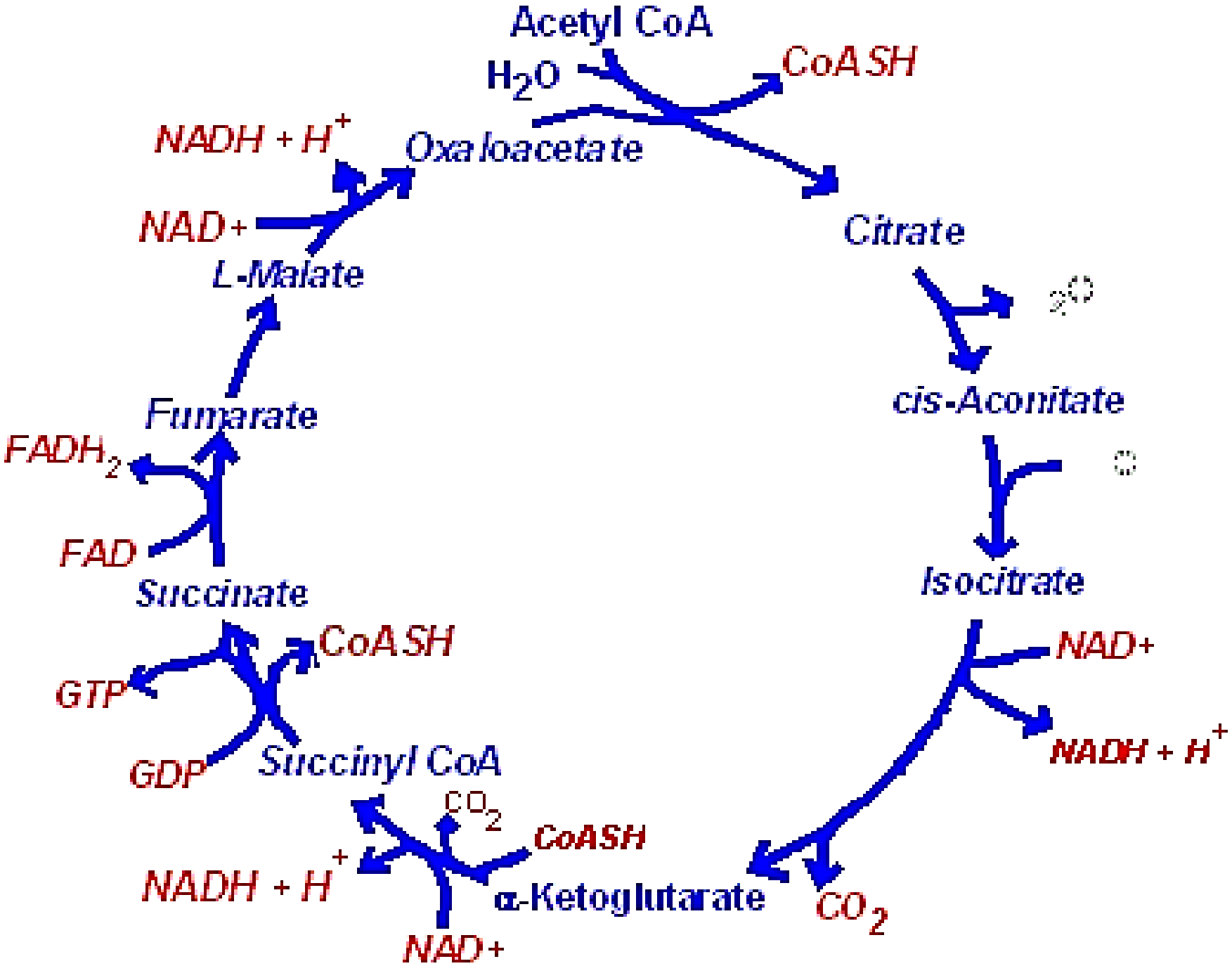

Acetyl-CoA
NADH + H+
CO2
PDH
NAD+
CoA
Pyruvate

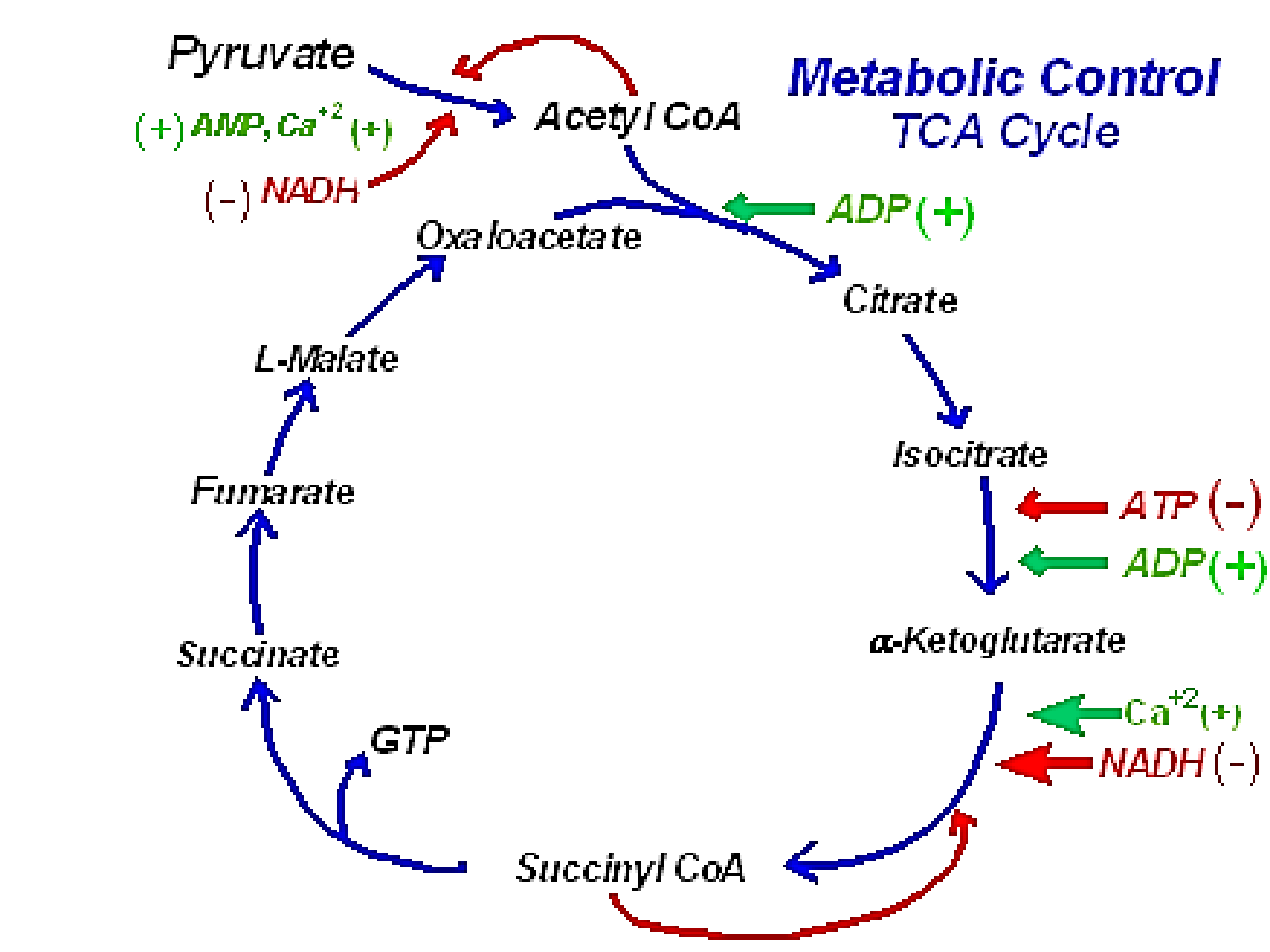
A


[Acetyl-CoA] / [CoA]
[NADH] / [NAD+]
[ATP] / [ADP]
Dichloroacetate
Ca2+
PDH KINASE
Pyruvate
Mg2+
ATP
ADP
PDH-a
(Active DEPHOSPHO-ENZYME)
PDH-b
(Inactive PHOSPHO-ENZYME)
P
Pi
H2O
PDH PHOSPHATASE
Mg2+, Ca2+
Insulin
(in adipose tissue)

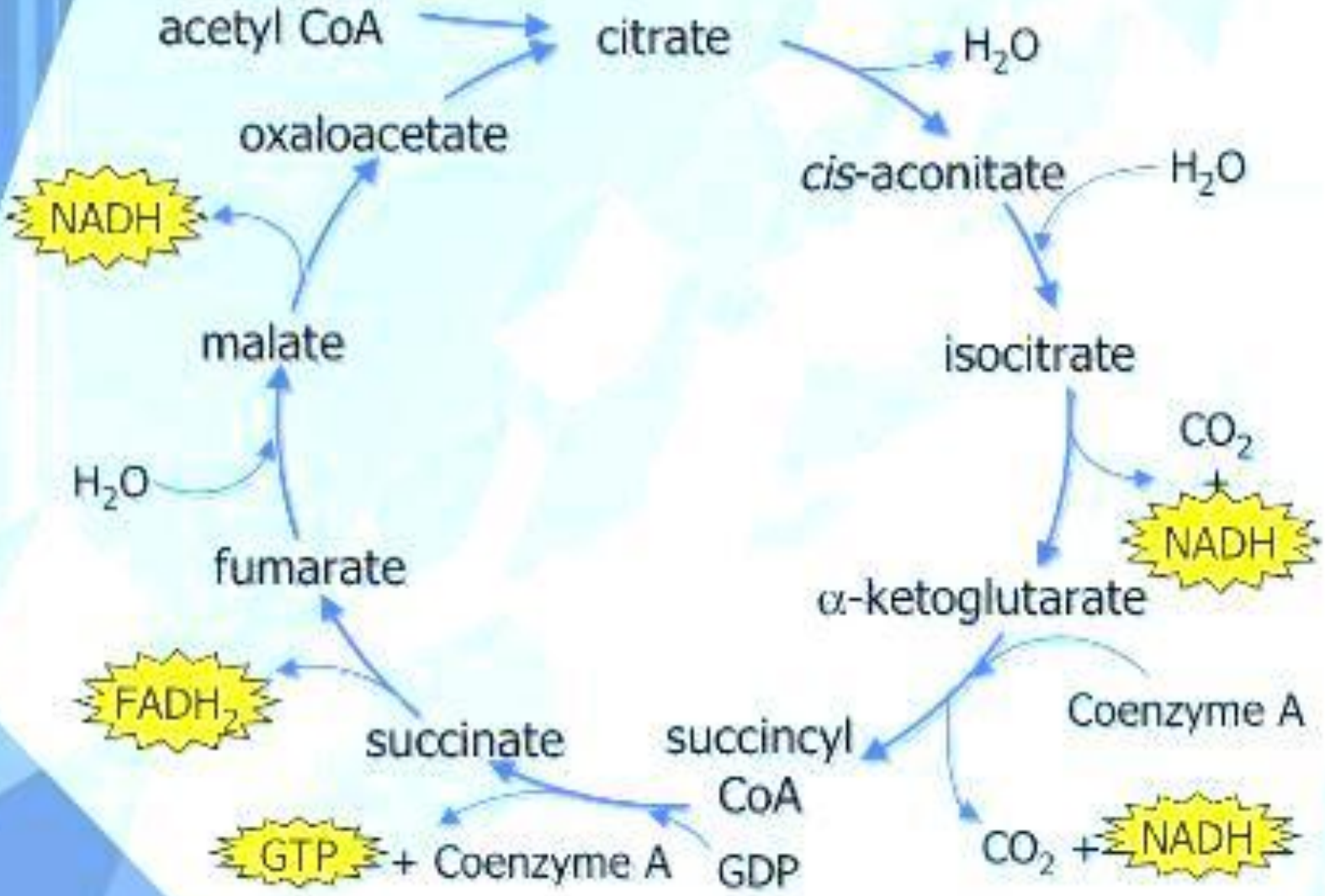
B


Pyruvate
Acetyl CoA
Fatty acids
Amino acids
carbohydrate
or
some amino acids
Tricarboxylic acid cycle
GTP
CO_2
CO_2
(4) $2H^+ + 2e^-$ (reducing equivalents)
Electron transport chain
Up to 11.5 ATP


Acetyl CoA
H_2O
CoASH
Oxaloacetate
$NADH + H^+$
$NAD+$
L-Malate
Citrate
cis-Aconitate
Isocitrate
$NAD+$
$NADH + H^+$
CO_2
α-Ketoglutarate
CoASH
$NADH + H^+$
$NAD+$
CO_2
Succinyl CoA
GTP
GDP
CoASH
Succinate
$FADH_2$
FAD
Fumarate


Metabolic Control
TCA Cycle
Pyruvate
(+) AMP, Ca+2 (+)
(–) NADH
Acetyl CoA
ADP (+)
Oxaloacetate
Citrate
L-Malate
Isocitrate
Fumarate
ATP (–)
ADP (+)
Succinate
α-Ketoglutarate
Ca+2 (+)
NADH (–)
GTP
Succinyl CoA

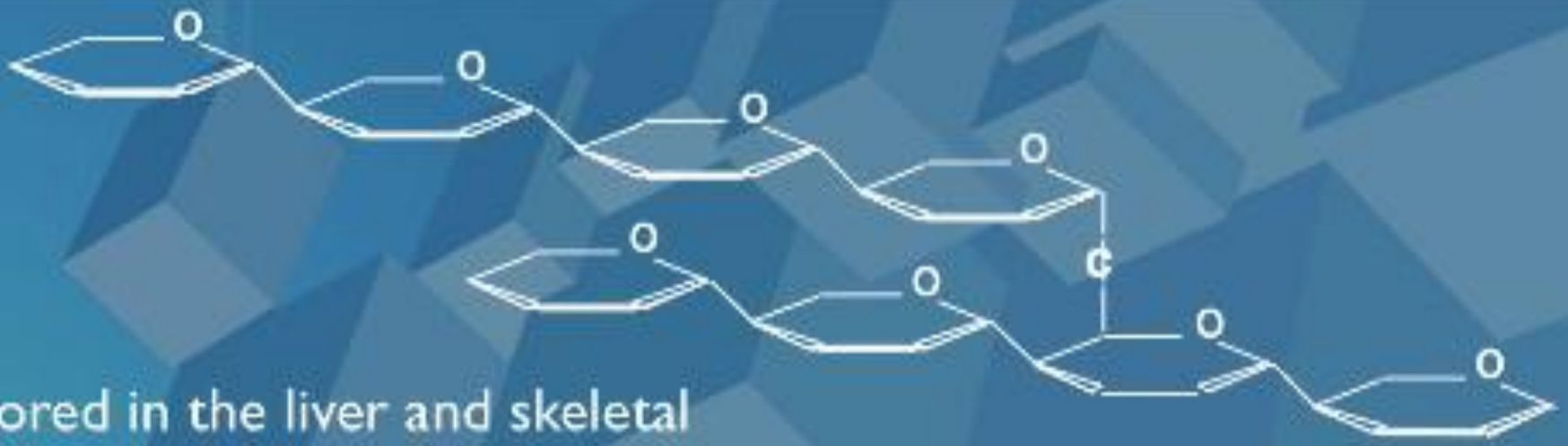
Energy & the citric acid cycle



Glycogen a glucose polymer that serves as the body's quick energy reserve.

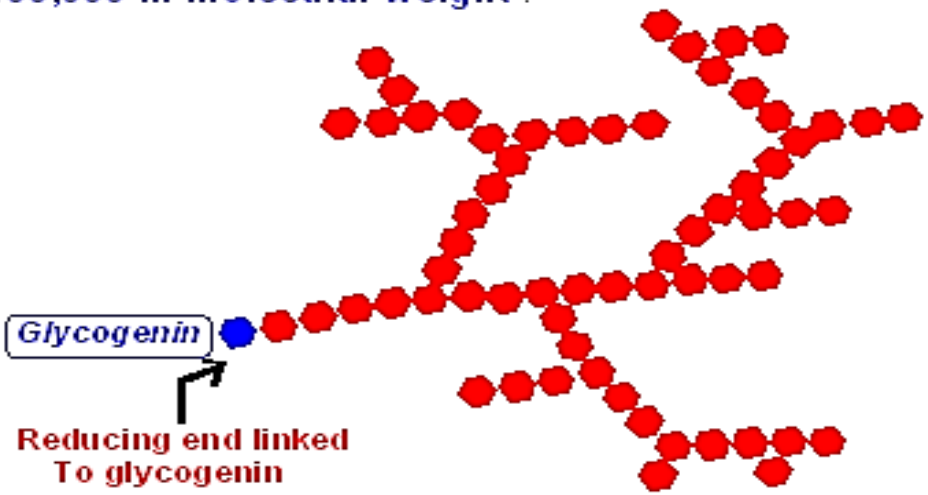
Average person usually maintains enough for one day's needs.

Glycogen

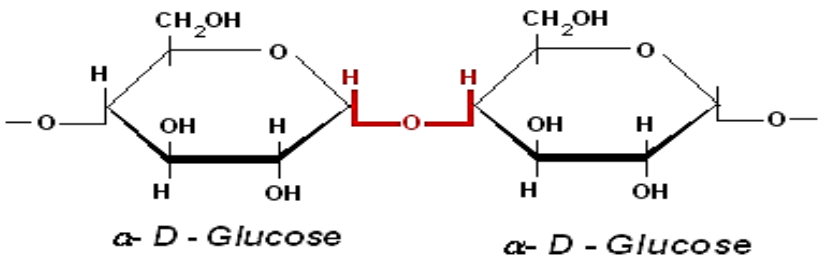


Stored in the liver and skeletal muscles as small granules.

Glycogen is a highly branched structure with an a [1 - 6] branch occurring approximately every 4th residue in the central core and less frequently in the outer branches. Mature glycogen molecules have very large molecular weights (up to 10,000,000) and are derived from proglycogen molecules of about 400,000 in molecular weight .

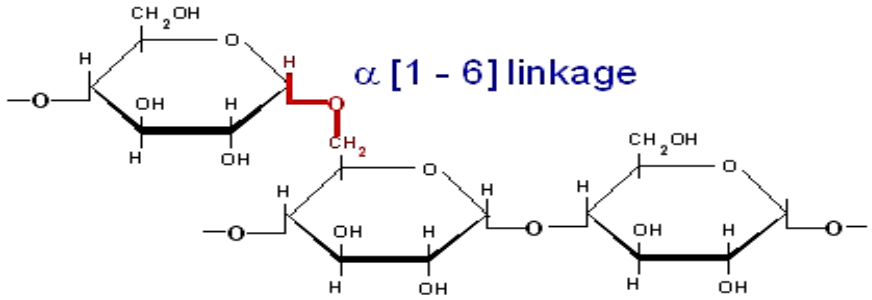


Glycogen is a polymer of glucose residues linked through α [1 - 4] and α [1 - 6] linkages

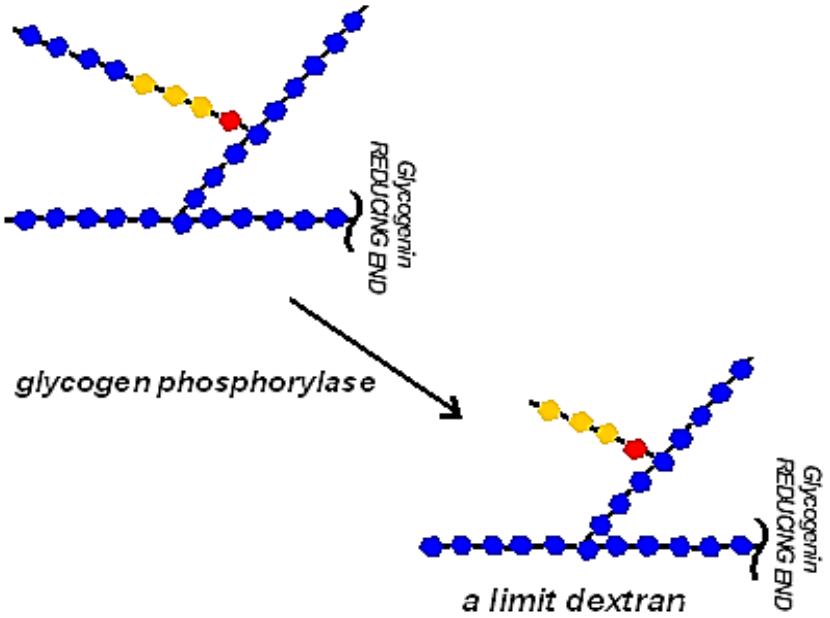


α [1 - 4] linkage

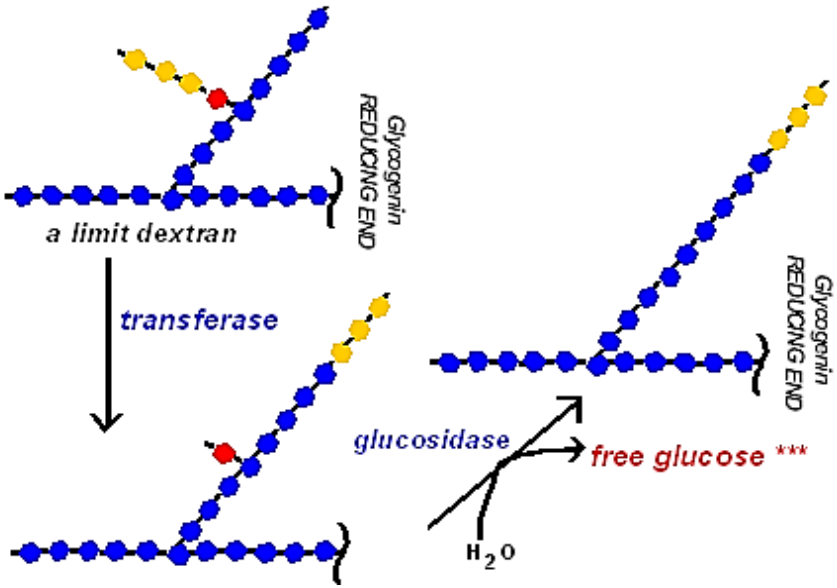
Glycogen is a polymer of glucose residues linked through α [1 - 4] and α [1 - 6] linkages

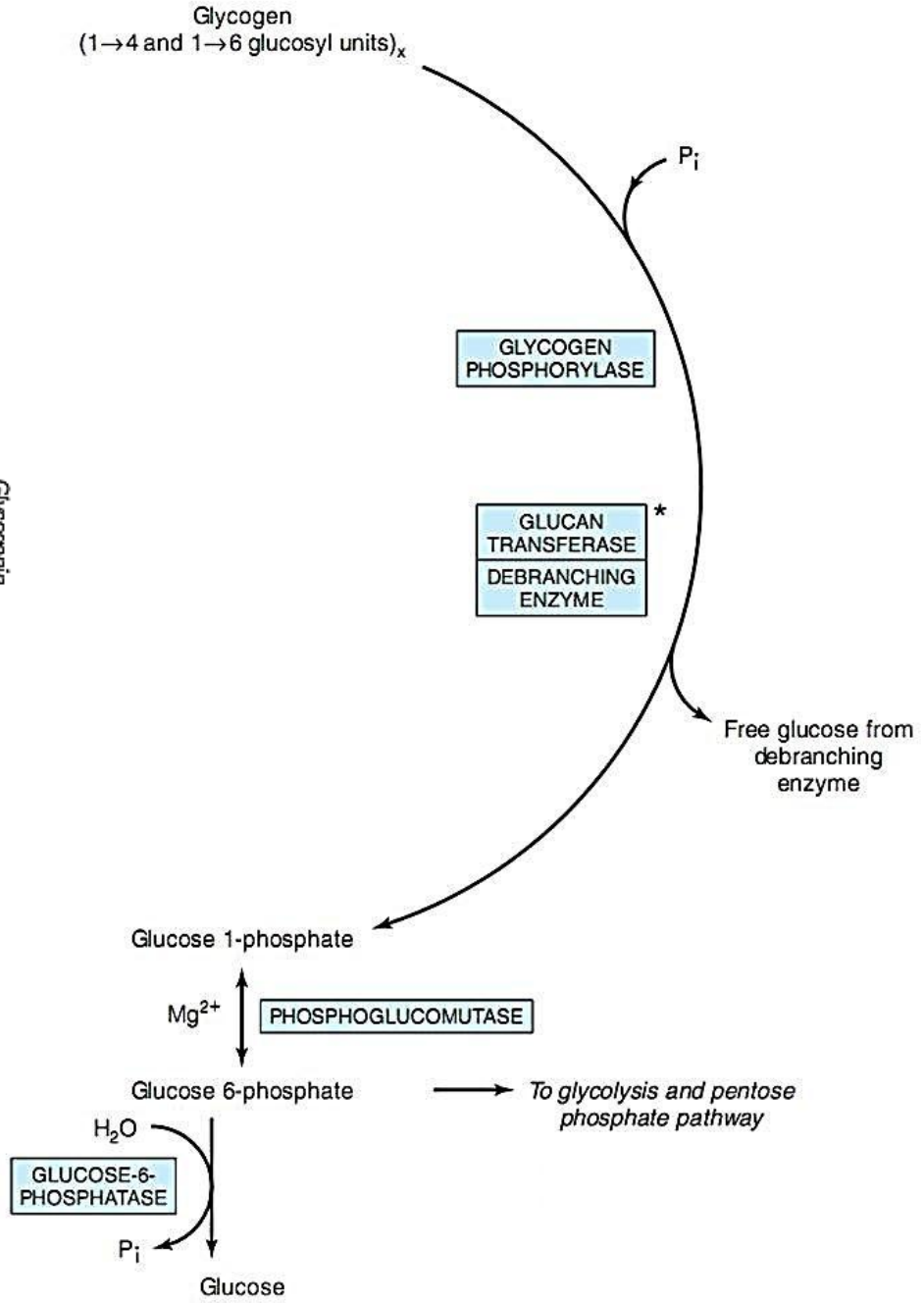


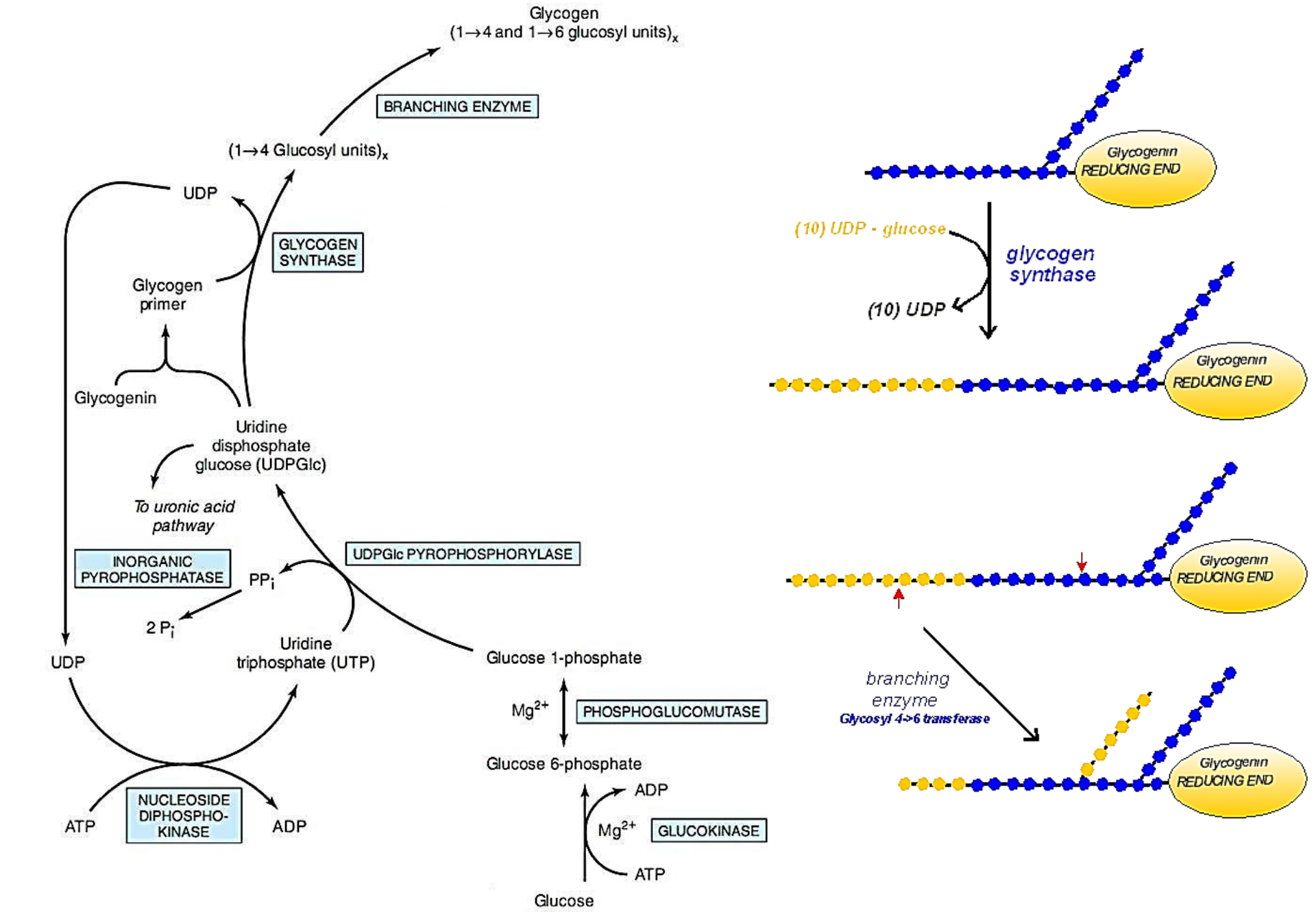
α [1 - 6] linkage

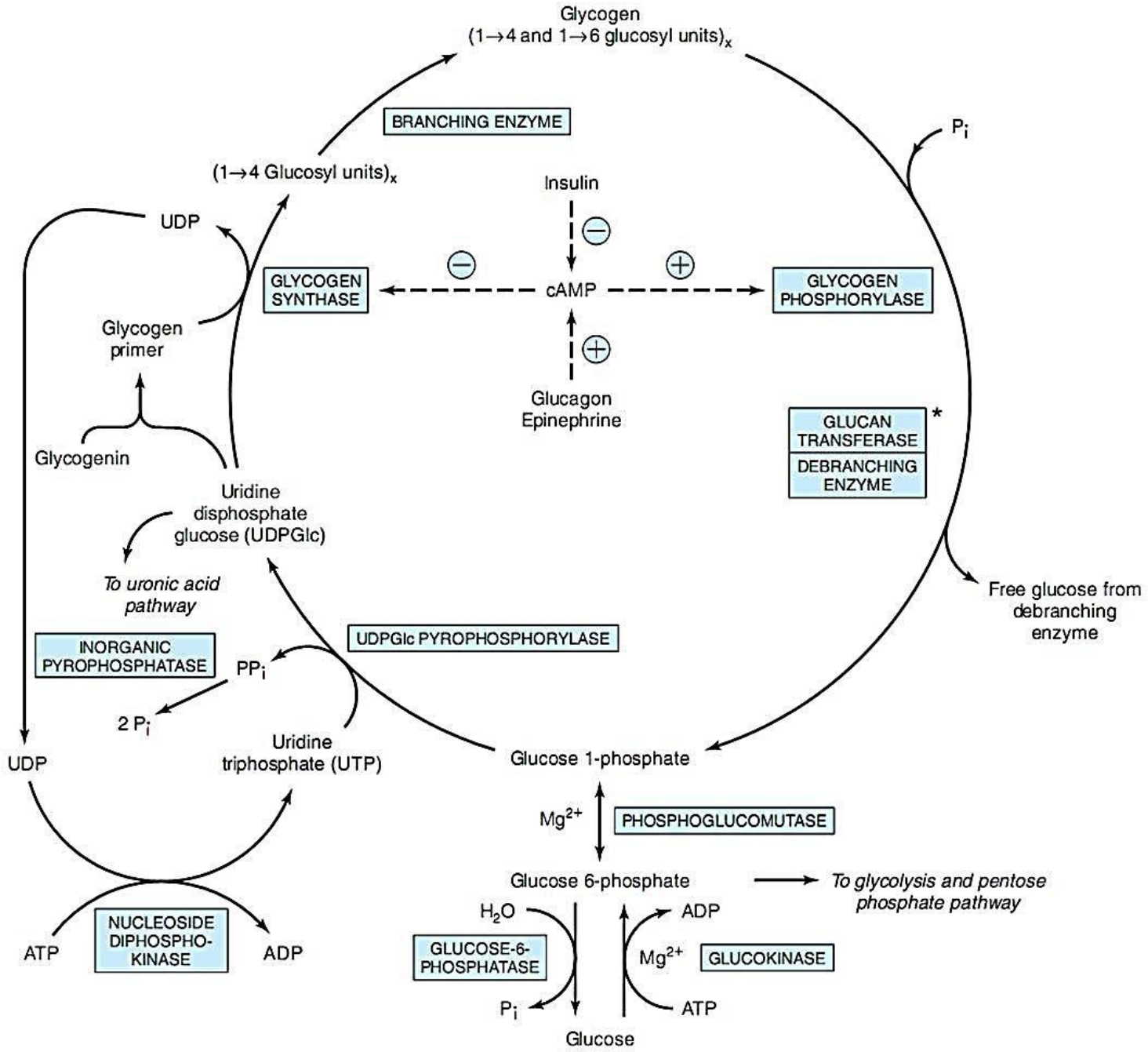


Actions of the Debranching Enzyme

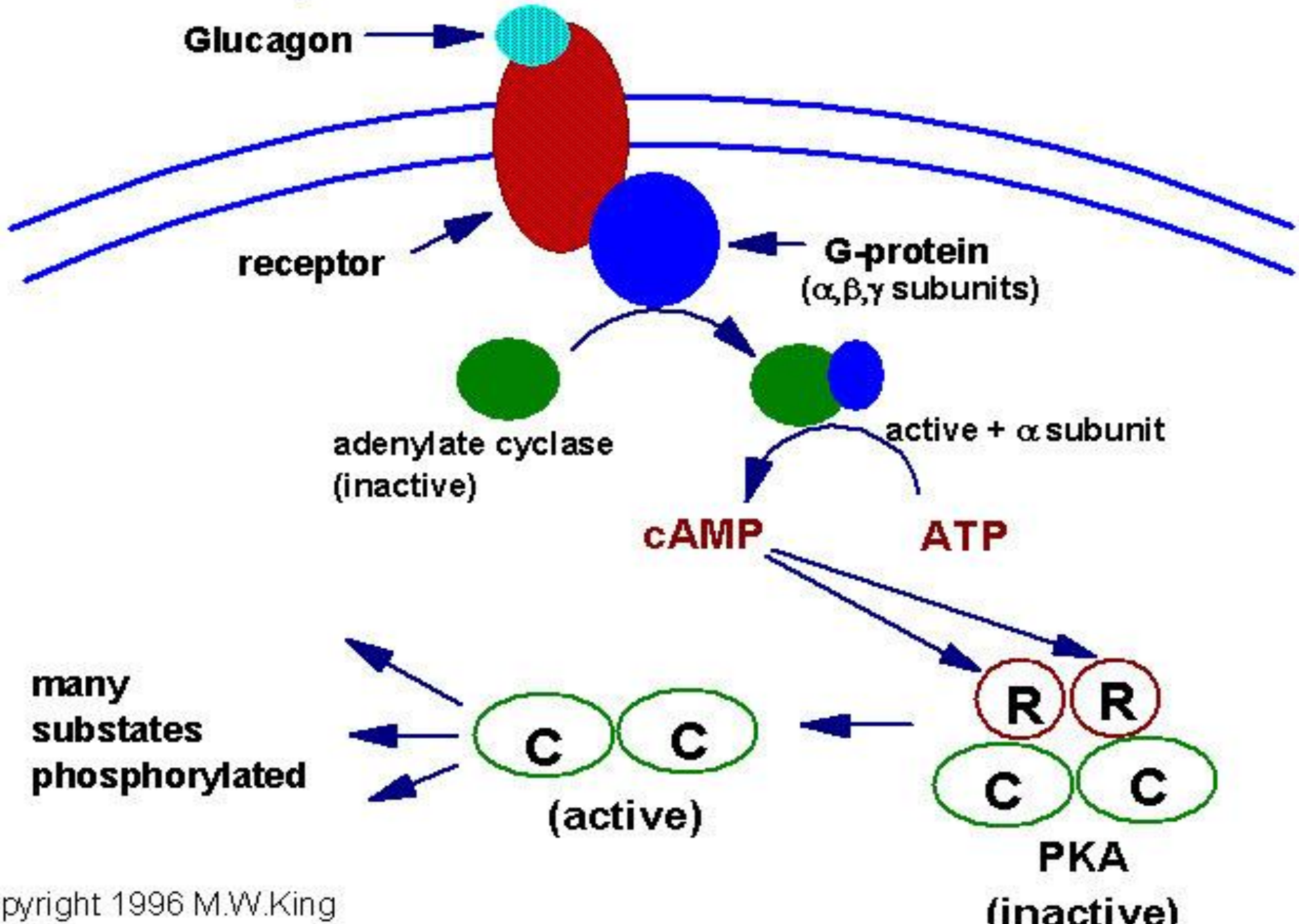


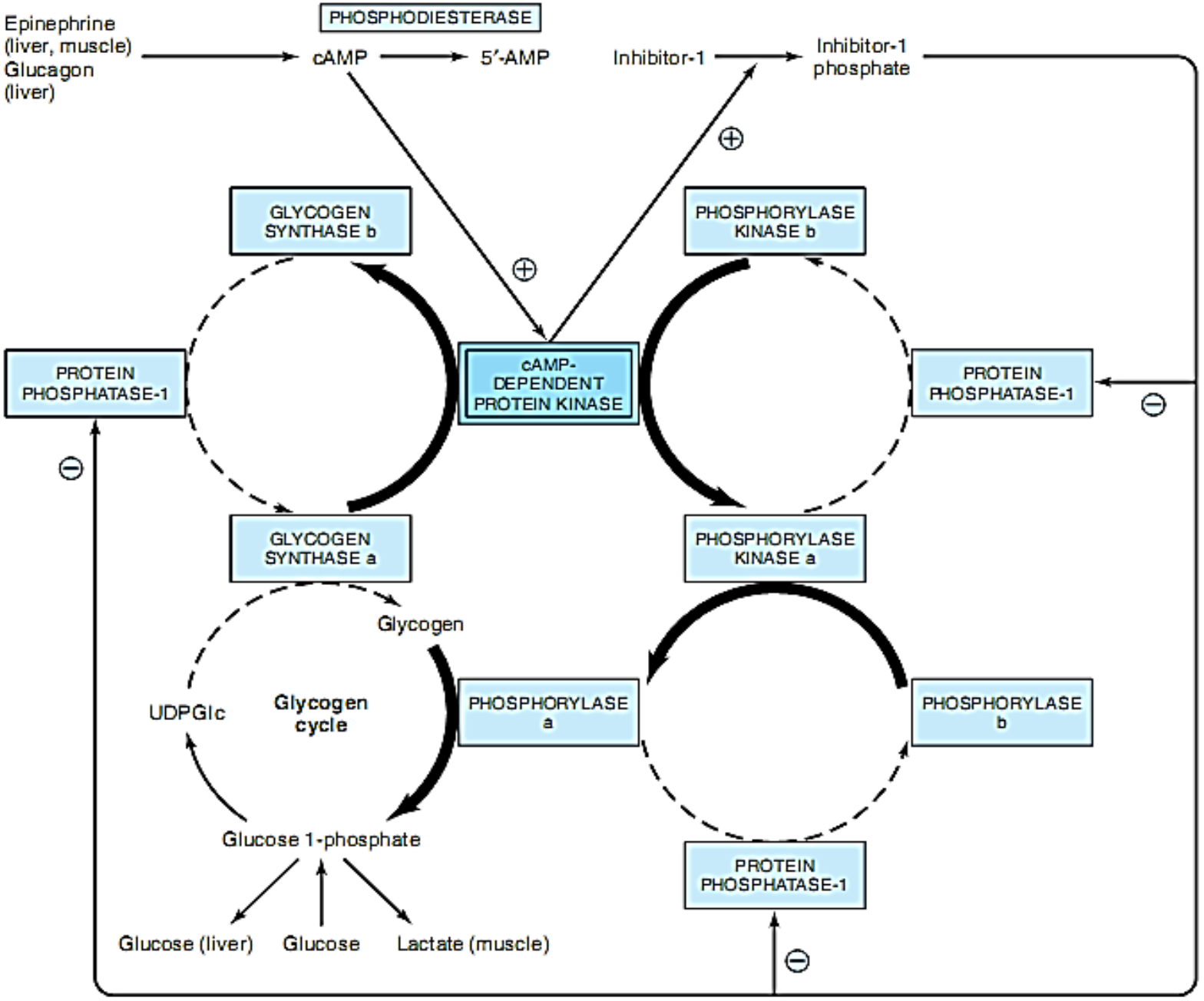


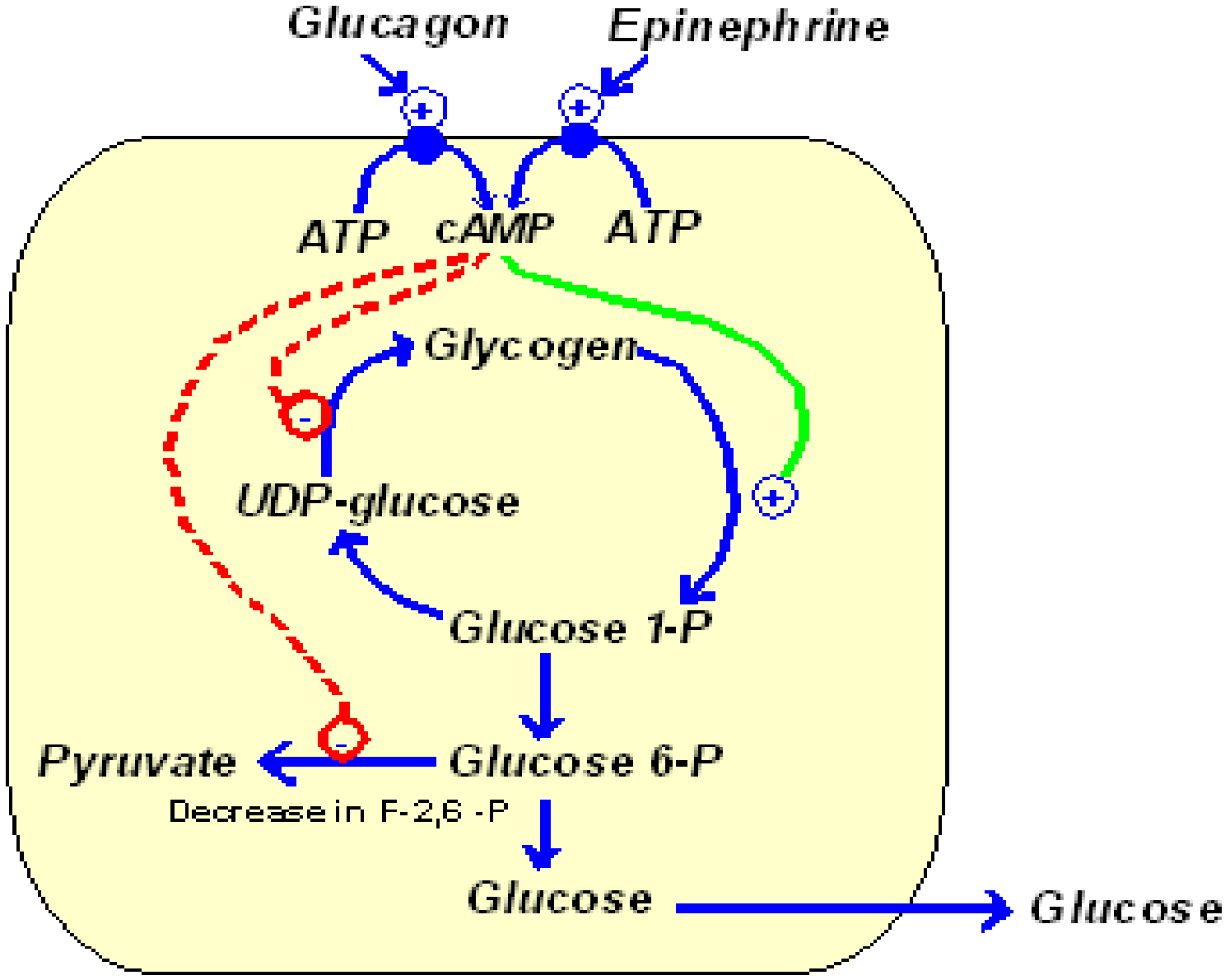

Glycogen
(1→4 and 1→6 glucosyl units)x
BRANCHING ENZYME
(1→4 Glucosyl units)x
UDP
GLYCOGEN SYNTHASE
Glycogen primer
Glycogenin
Uridine disphosphate glucose (UDPGlc)
To uronic acid pathway
INORGANIC PYROPHOSPHATASE
PPi
2 Pi
UDPGlc PYROPHOSPHORYLASE
UDP
Uridine triphosphate (UTP)
Glucose 1-phosphate
Mg2+
PHOSPHOGLUCOMUTASE
Glucose 6-phosphate
ATP
NUCLEOSIDE DIPHOSPHO-KINASE
ADP
ADP
Mg2+
GLUCOKINASE
ATP
Glucose
Glycogenin REDUCING END
(10) UDP - glucose
glycogen synthase
(10) UDP
Glycogenin REDUCING END
Glycogenin REDUCING END
branching enzyme
Glycosyl 4->6 transferase
Glycogenin REDUCING END

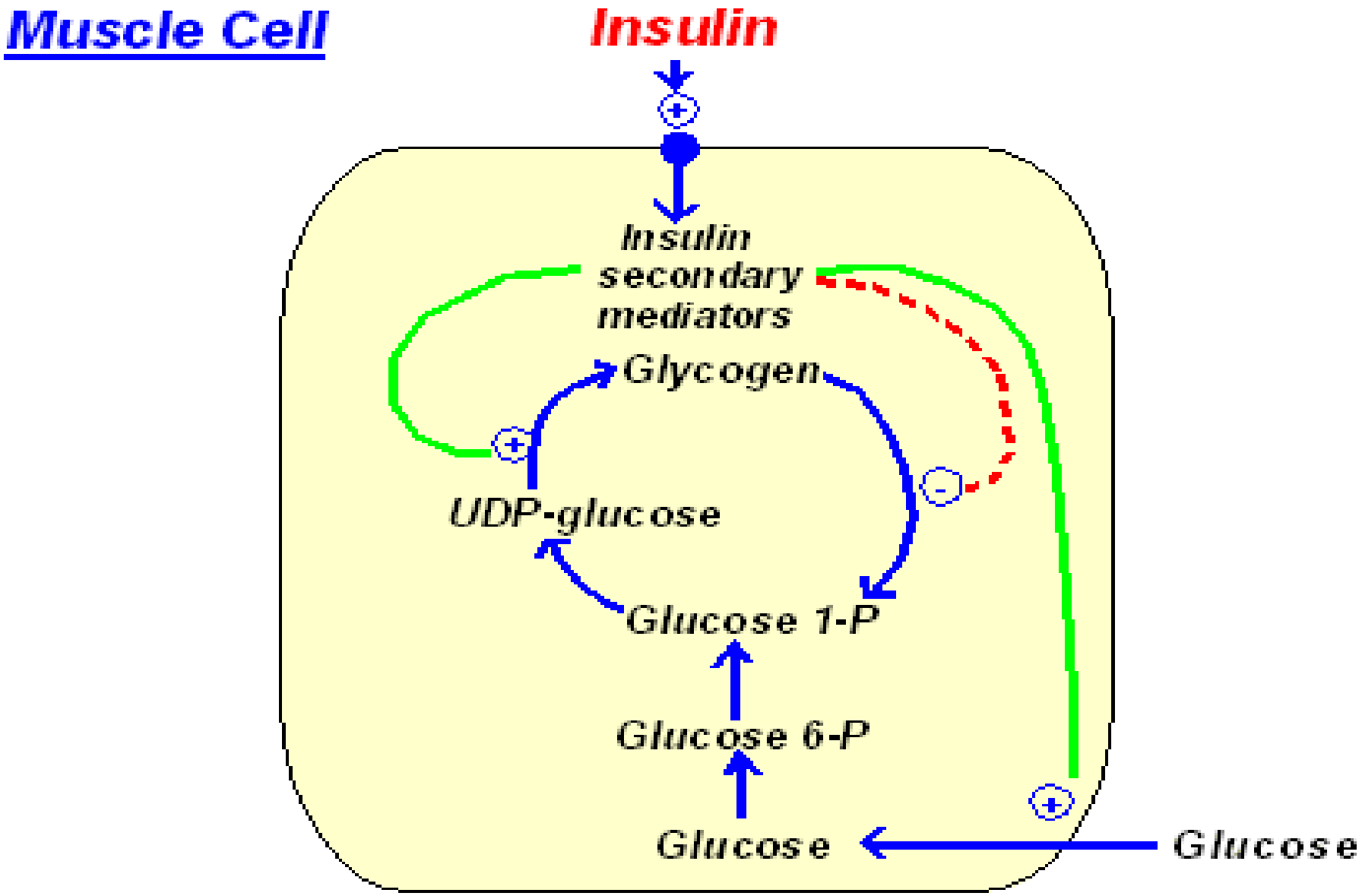

Glycogen
(1→4 and 1→6 glucosyl units)x
BRANCHING ENZYME
(1→4 Glucosyl units)x
Pi
Insulin
UDP
GLYCOGEN SYNTHASE
cAMP
GLYCOGEN PHOSPHORYLASE
Glycogen primer
Glucagon
Epinephrine
GLUCAN TRANSFERASE
DEBRANCHING ENZYME
*
Glycogenin
Uridine disphosphate glucose (UDPGlc)
To uronic acid pathway
Free glucose from debranching enzyme
INORGANIC PYROPHOSPHATASE
PPi
UDPGlc PYROPHOSPHORYLASE
2 Pi
UDP
Uridine triphosphate (UTP)
Glucose 1-phosphate
Mg2+
PHOSPHOGLUCOMUTASE
Glucose 6-phosphate
To glycolysis and pentose phosphate pathway
H2O
ADP
GLUCOSE-6-PHOSPHATASE
Mg2+
GLUCOKINASE
Pi
ATP
Glucose
ATP
NUCLEOSIDE DIPHOSPHO-KINASE
ADP

Receptor-Mediated Activation of PKA

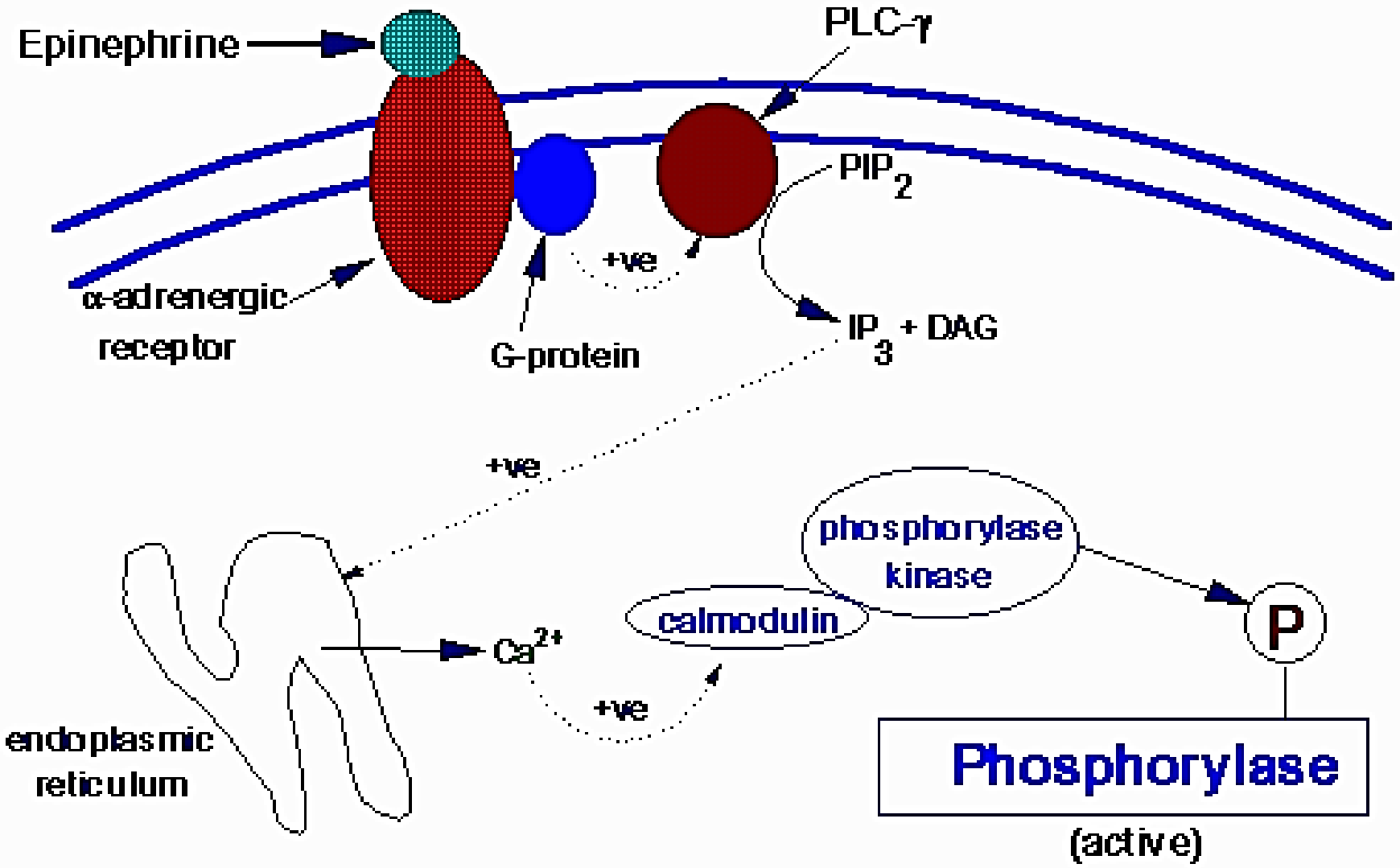



Epinephrine
(liver, muscle)
Glucagon
(liver)
PHOSPHODIESTERASE
cAMP
5′-AMP
Inhibitor-1
Inhibitor-1
phosphate
GLYCOGEN
SYNTHASE b
PHOSPHORYLASE
KINASE b
PROTEIN
PHOSPHATASE-1
cAMP-
DEPENDENT
PROTEIN KINASE
PROTEIN
PHOSPHATASE-1
GLYCOGEN
SYNTHASE a
PHOSPHORYLASE
KINASE a
Glycogen
UDPGlc
Glycogen
cycle
PHOSPHORYLASE
a
PHOSPHORYLASE
b
Glucose 1-phosphate
PROTEIN
PHOSPHATASE-1
Glucose (liver)
Glucose
Lactate (muscle)

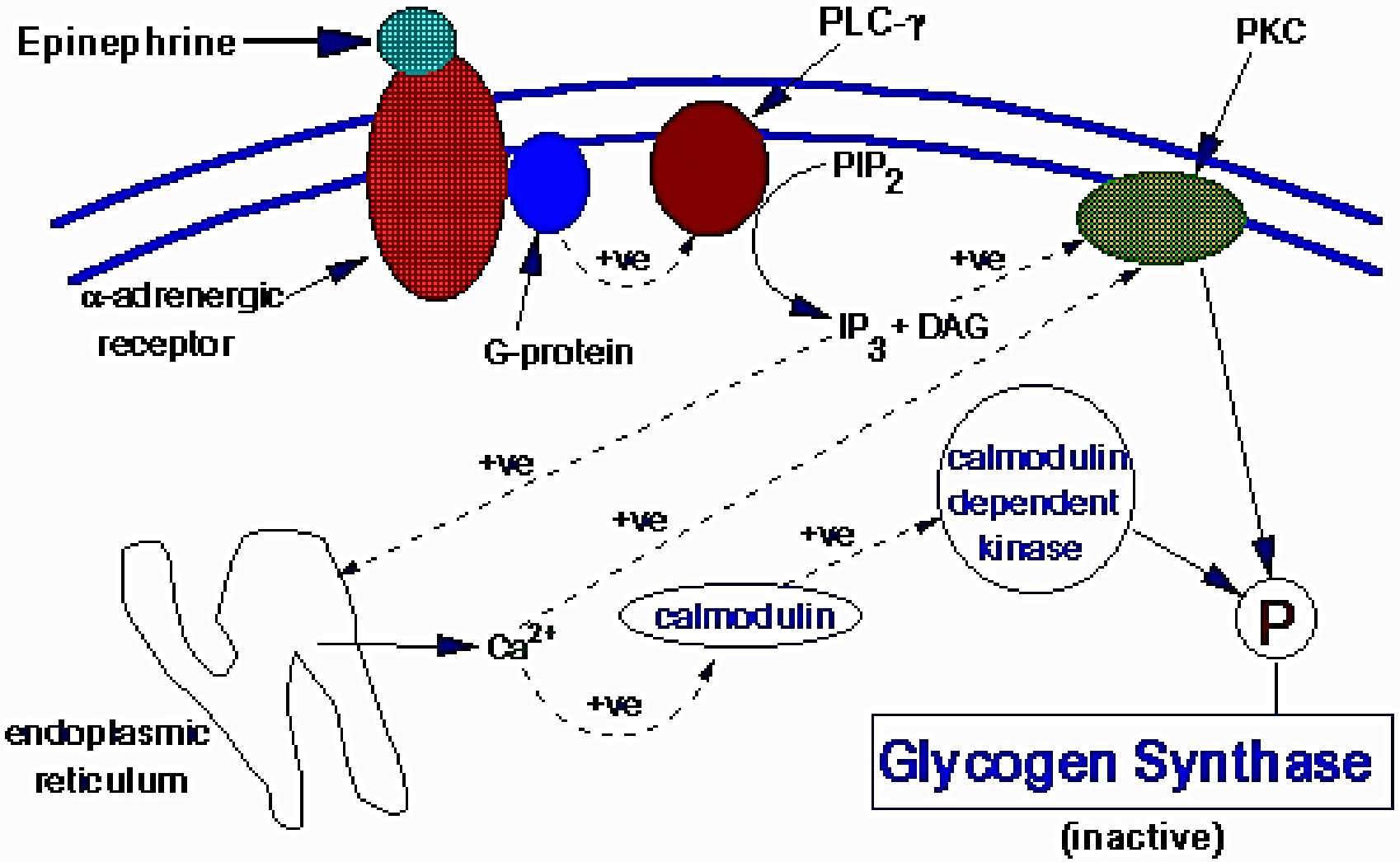

Glucagon
Epinephrine
ATP
cAMP
ATP
Glycogen
UDP-glucose
Glucose 1-P
Pyruvate
Glucose 6-P
Decrease in F-2,6 -P
Glucose
Glucose


Muscle Cell
Insulin
Insulin
secondary
mediators
Glycogen
UDP-glucose
Glucose 1-P
Glucose 6-P
Glucose
Glucose

α-Receptor-Mediated Responses on Phosphorylase

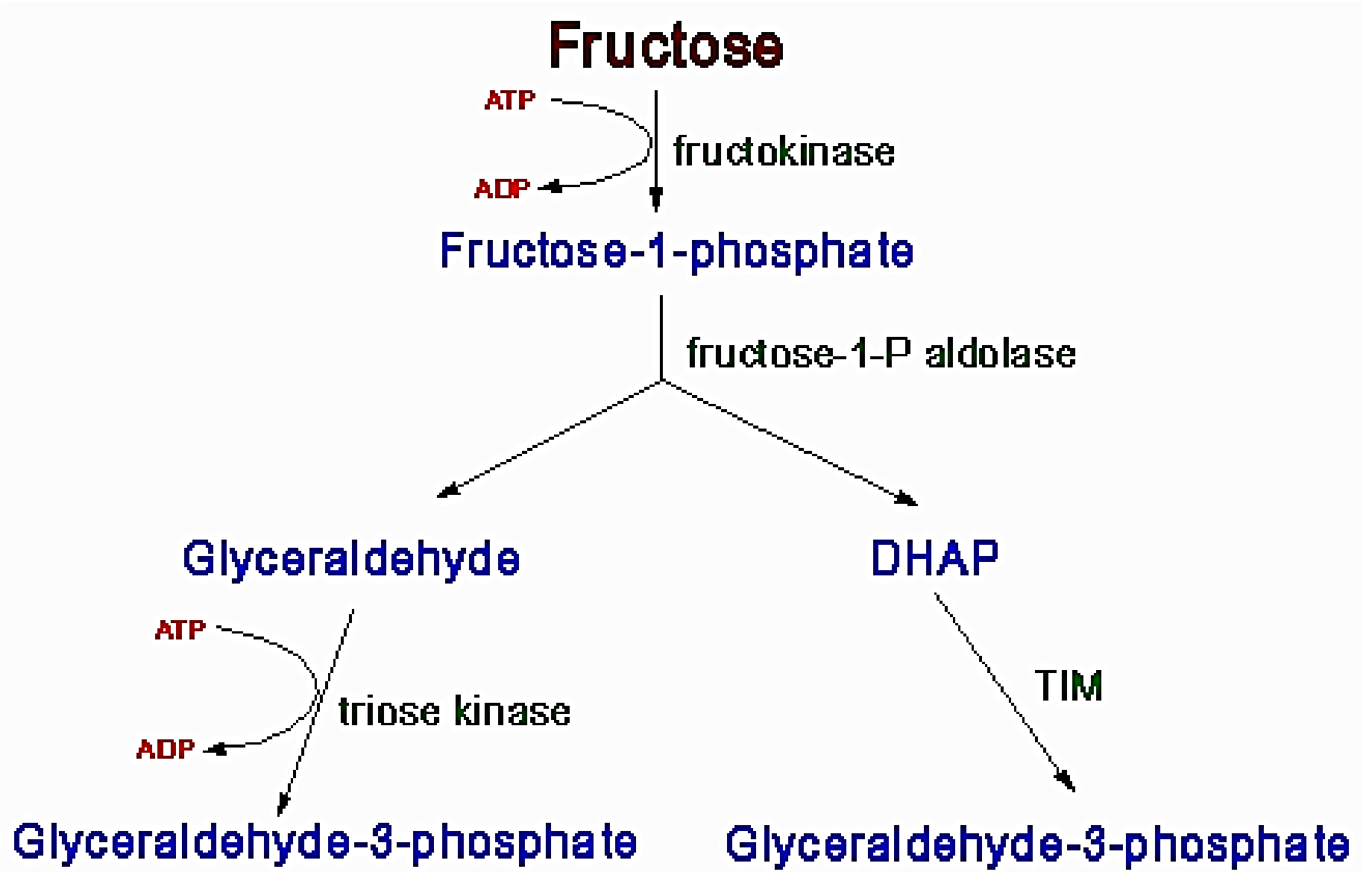


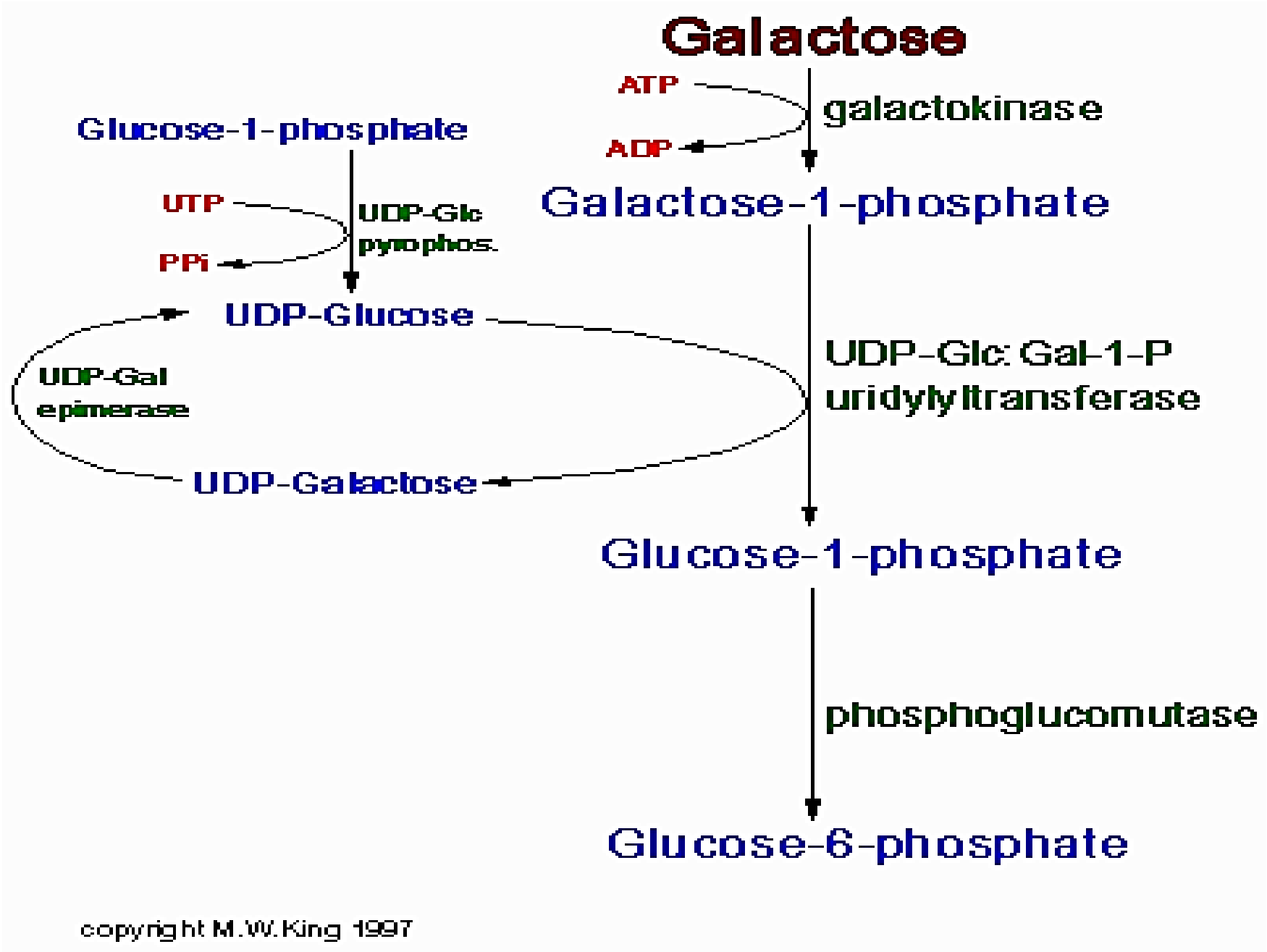
α-Receptor-Mediated Responses on Glycogen Synthase



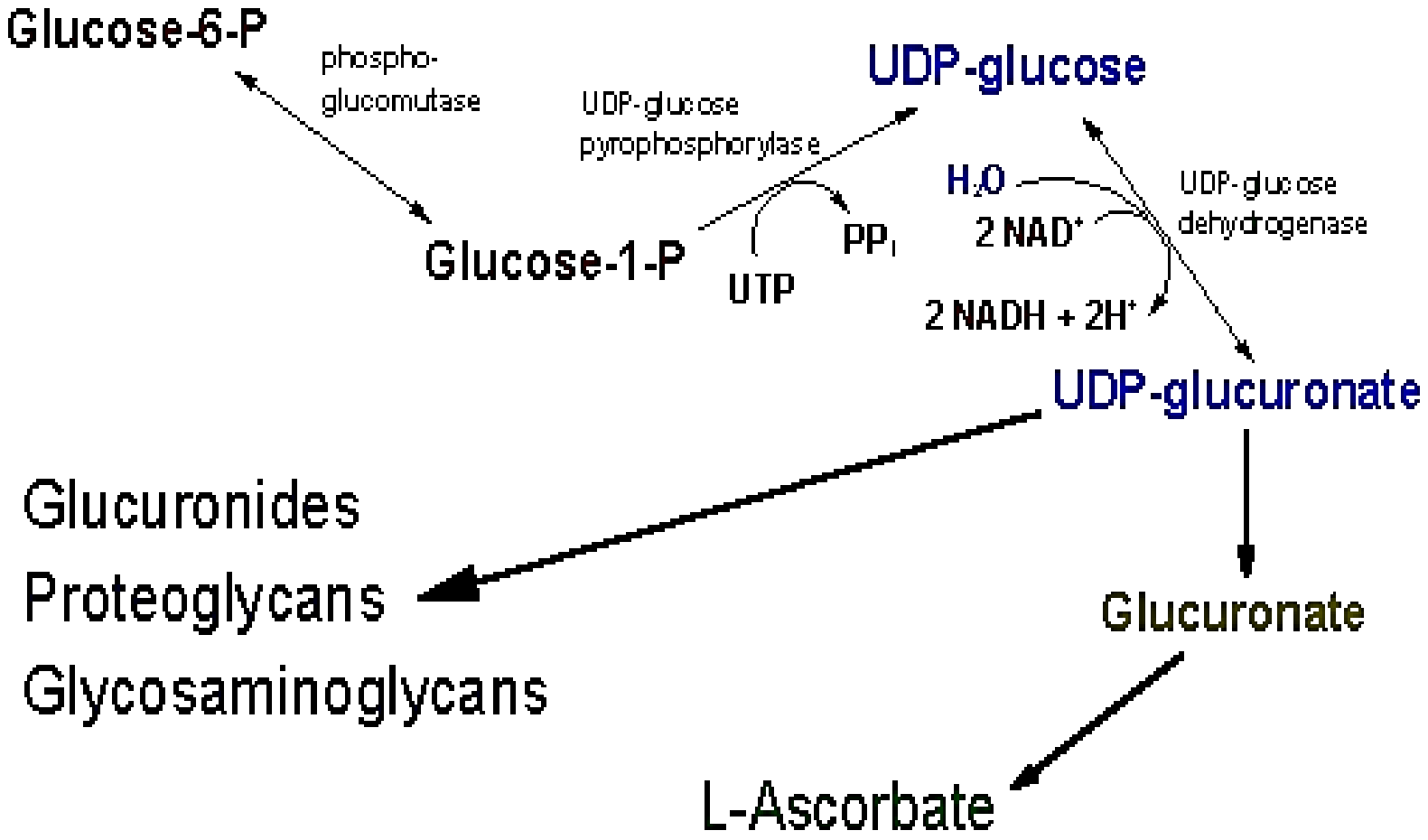
Glycogen Storage Diseases

Glycogenosis	Name	Cause of Disorder	Characteristics
Type I	Von Gierke's disease	Deficiency of glucose-6-phosphatase	Liver cells and renal tubule cells loaded with glycogen. Hypoglycemia, lactic-acidemia, ketosis, hyperlipemia.
Type II	Pompe's disease	Deficiency of lysosomal α-1→4- and 1→6-glucosidase (acid maltase)	Fatal, accumulation of glycogen in lysosomes, heart failure.
Type III	Limit dextrinosis, Forbes' or Cori's disease	Absence of debranching enzyme	Accumulation of a characteristic branched polysaccharide.
Type IV	Amylopectinosis, Andersen's disease	Absence of branching enzyme	Accumulation of a polysaccharide having few branch points. Death due to cardiac or liver failure in first year of life.
Type V	Myophosphorylase deficiency, McArdle's syndrome	Absence of muscle phosphorylase	Diminished exercise tolerance; muscles have abnormally high glycogen content (2.5–4.1%). Little or no lactate in blood after exercise.
Type VI	Hers' disease	Deficiency of liver phosphorylase	High glycogen content in liver, tendency toward hypoglycemia.
Type VII	Tarui's disease	Deficiency of phosphofructokinase in muscle and erythrocytes	As for type V but also possibility of hemolytic anemia.
Type VIII		Deficiency of liver phosphorylase kinase	As for type VI.





Glucuronic Acid Synthesis



An Alternate Pathway for the Oxidation of Glucose

The Pentose Phosphate or Hexose Monophosphate Shunt Pathway

The Pentose Phosphate Pathway Provides:

NADPH

Required for many biosynthetic reactions (reductions)

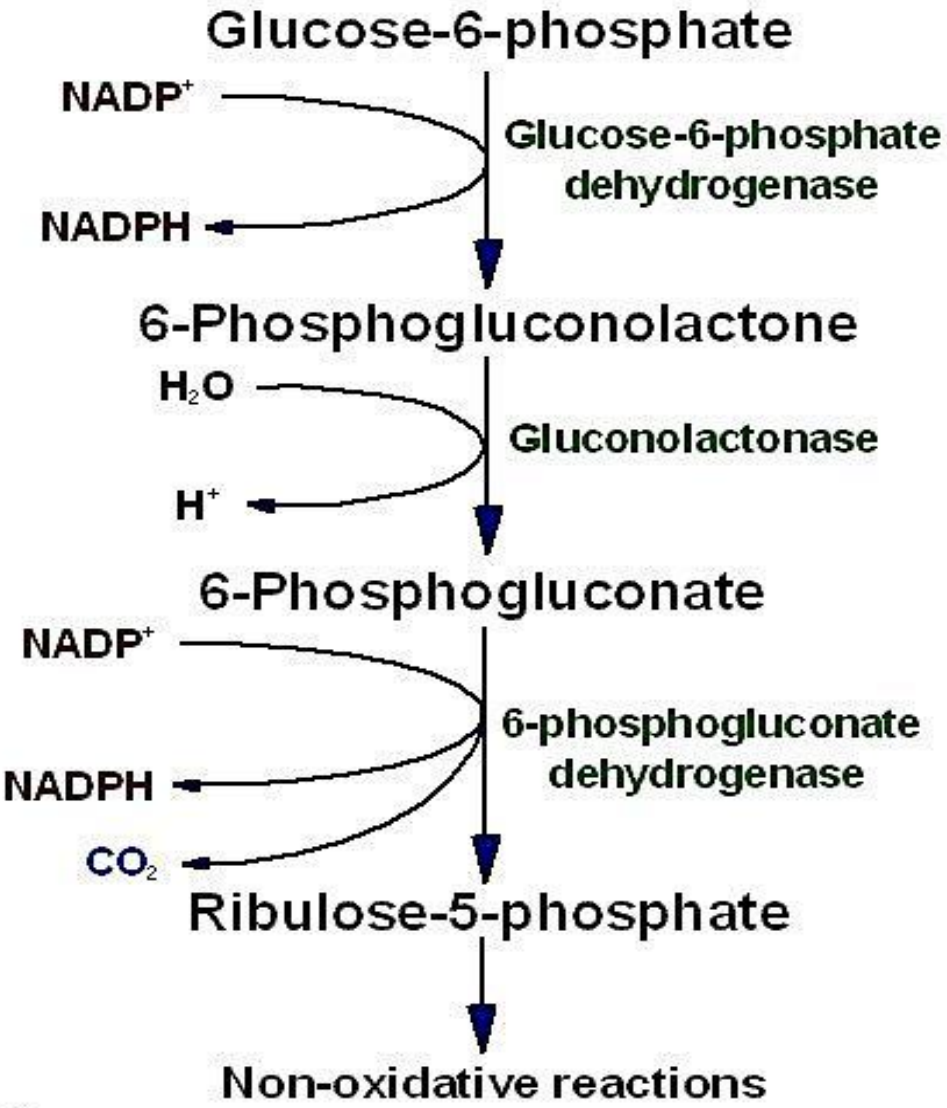
Necessary for maintenance of reduced glutathione in red blood cells and the reduction of methemoglobin.

Various tissues utilize this pathway to different degrees depending on their requirements for NADPH and Ribose 5-phosphate

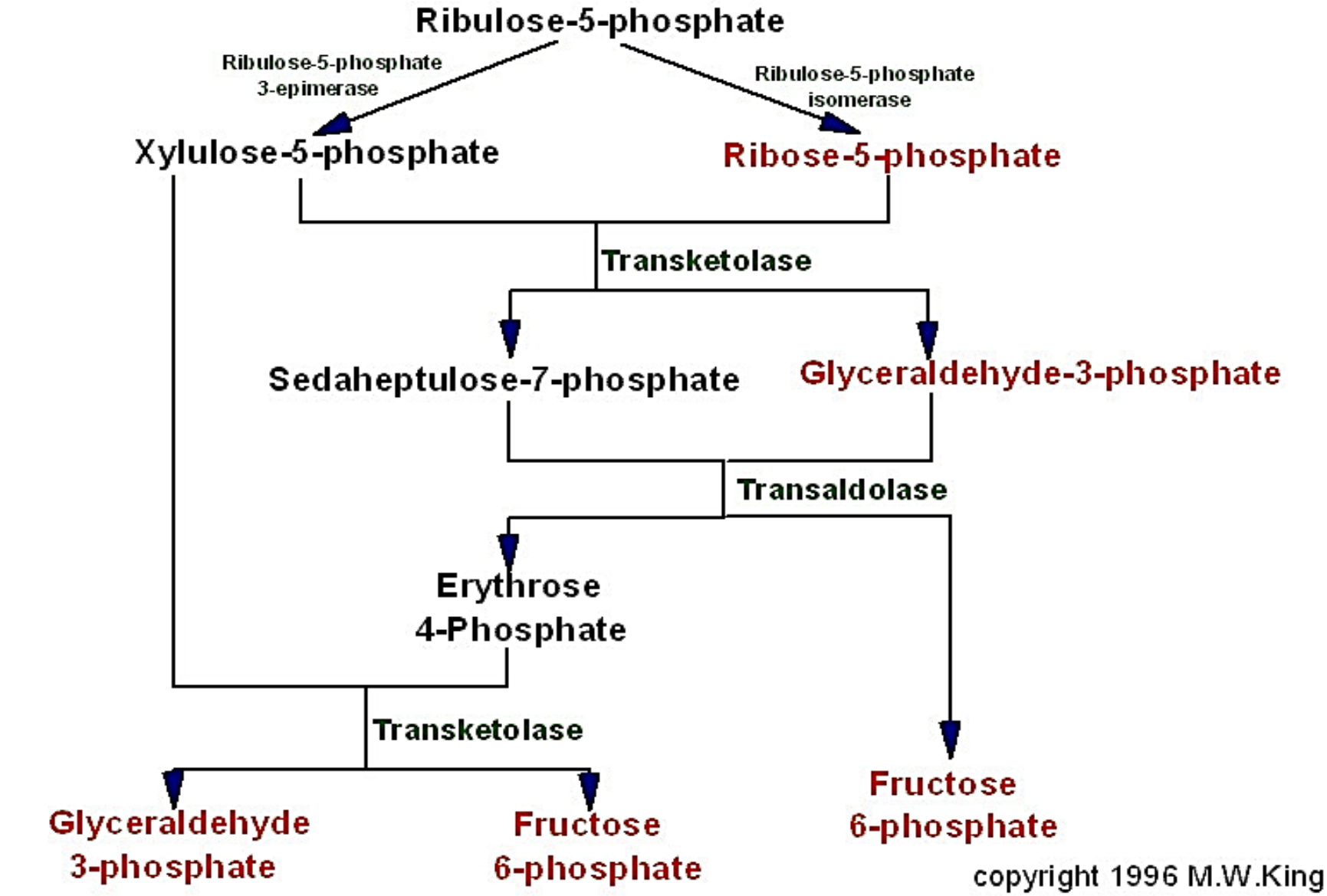
Ribose 5-phosphate

Necessary for nucleotide and cofactor biosynthesis

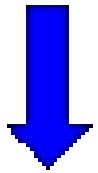
Oxidative Stage of Pentose Phosphate Pathway



Non-Oxidative Stage of Pentose Phosphate Pathway



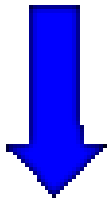
$$6\ Glucose\ 6\text{-}phosphate + 12\ NADP^{+} + 7\ H_2O$$



$$5\ Glucose\ 6\text{-}phosphate + 12\ NADPH + 6\ CO_2 + 12\ H^{+} + P_i$$

Net Reaction:

$$Glucose\ 6\text{-}phosphate + 12\ NADP^{+} + 7\ H_2O$$



$$12\ NADPH + 6\ CO_2 + 12\ H^{+} + P_i$$

G6PD Abnormalities